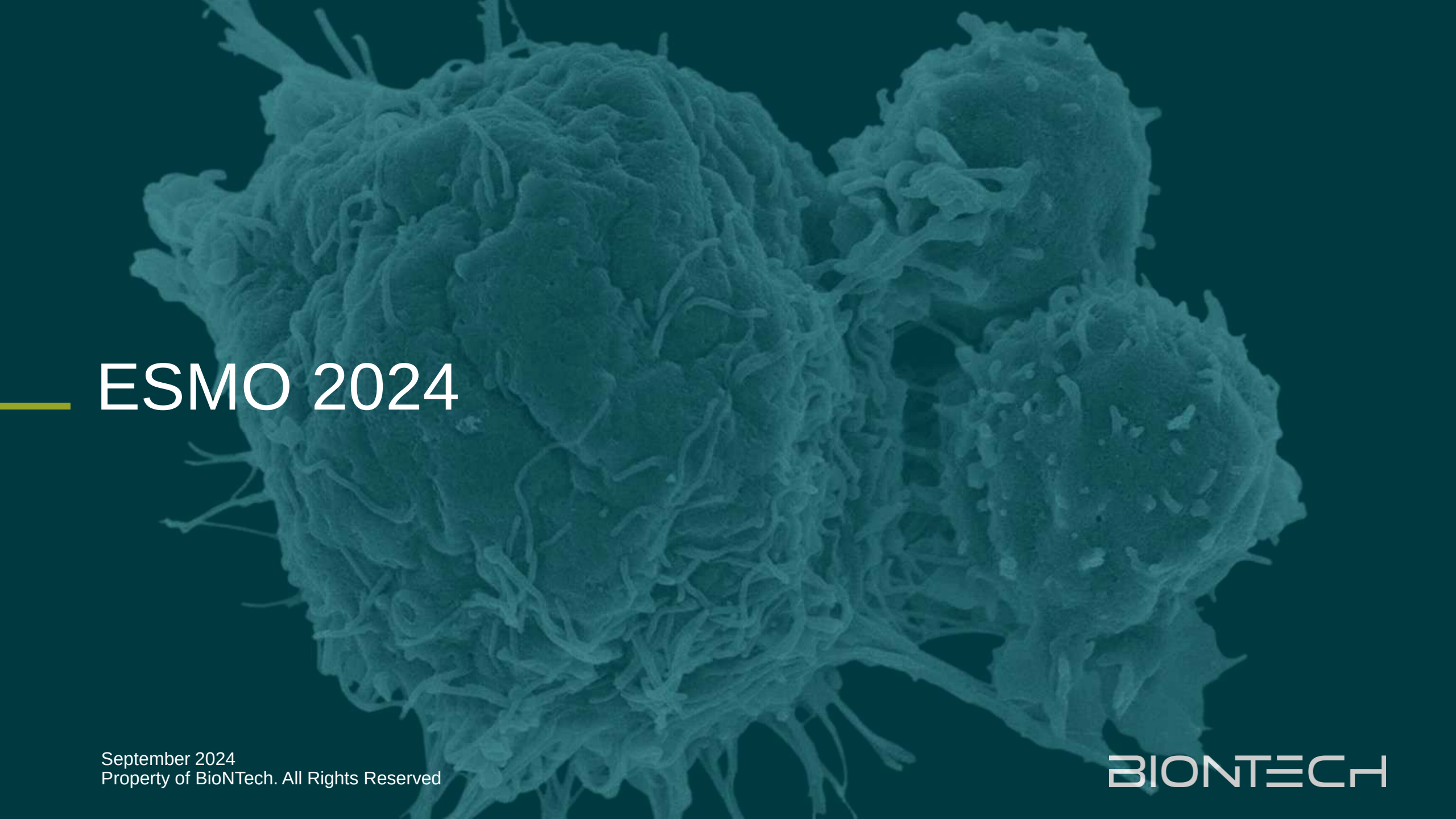

ESMO 2024

September 2024

This Slide Presentation Includes Forward-Looking Statements

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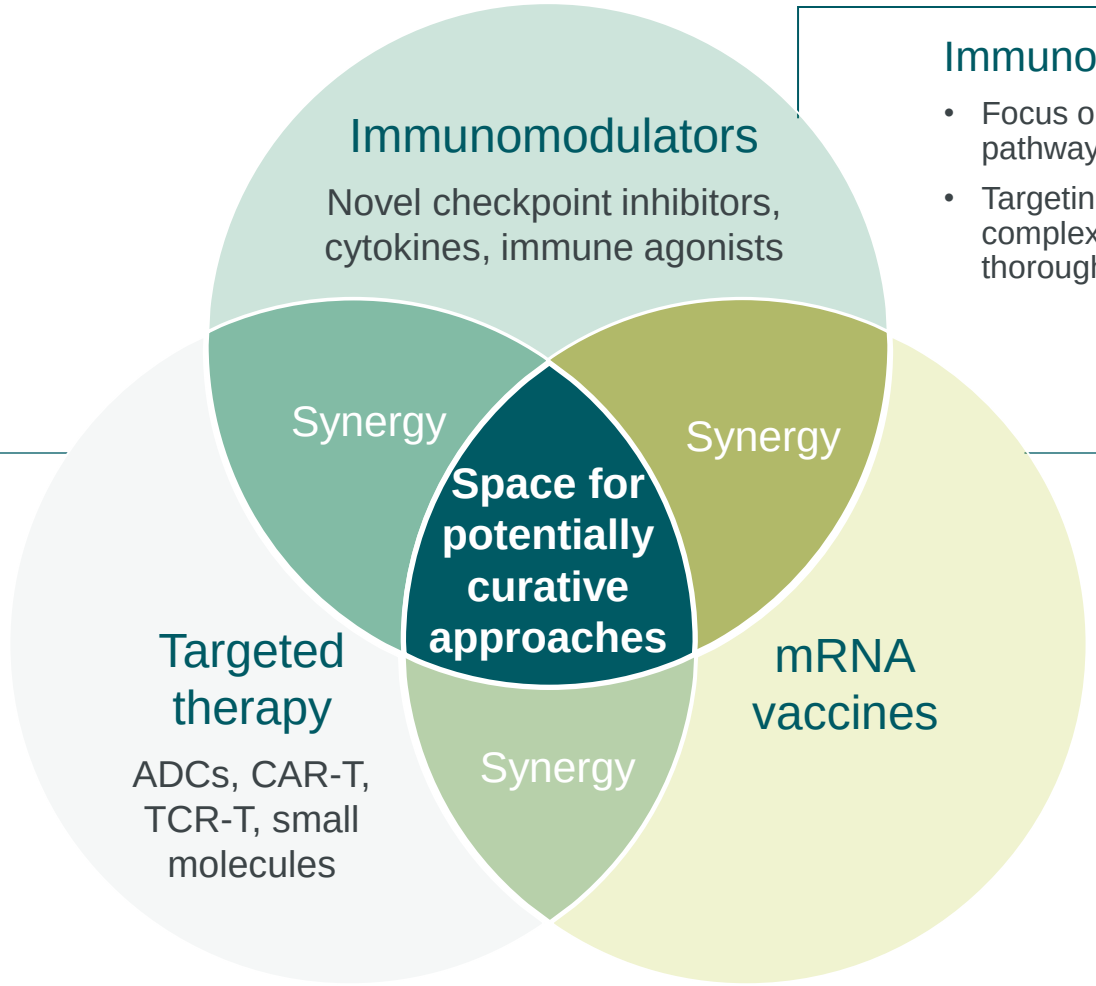
Towards An Approach to Cancer based on Multiple Modalities and Differentiated Novel/Novel Therapeutic Combinations

Immunomodulators

- Focus on the most relevant and crucial IO pathways
- Targeting different complementary players in the complex cancer immunity cycle may promote a thorough and durable anti-tumor effect



Targeted therapy

- Potent and precise therapies could rapidly reduce tumor burden
- Designed to have clinical efficacy across the entire disease continuum including late lines

mRNA cancer vaccines

- Could eliminate polyclonal residual disease with individualized vaccines for potential long-term impact
- Polyspecific activity by targeting multiple antigens at once

ADC = antibody-drug conjugate; CAR = chimeric antigen receptor; TCR-T = T-cell receptor engineered T cell; IO = immune oncology.

BIONTECH

Our Multi-modality Immuno-Oncology Pipeline Today

Phase 1	Phase 1/2	Phase 2	Phase 3
BNT116 Adv. NSCLC	**BNT142** (CD3xCLDN6) Multiple CLDN6-pos. adv. solid tumors	**BNT111**[6] aPD-(L)1-R/R melanoma, + cemiplimab	**BNT316/ONC-392 (gotistobart)**[4] (CTLA-4) aPD-(L)1 experienced NSCLC
Autogene cevumeran (BNT122)[1] Multiple solid tumors	**BNT311/GEN1046 (acasunlimab)**[2] **(**PD-L1x4-1BB) Multiple solid tumors	**BNT113** 1L rel./met. HPV16+ PD-L1+ head and neck cancer, + pembrolizumab	**BNT323/DB-1303**[5] (HER2) HR+/HER2-low met. breast cancer
BNT152 + BNT153 (IL-7, IL-2) Multiple solid tumors	**BNT312/GEN1042**[2] (CD40x4-1BB) Multiple solid tumors	**BNT116**[6] 1L adv. PD-L1 ≥ 50% NSCLC, + cemiplimab	
BNT211 (CLDN6) Multiple solid tumors	**BNT314/GEN1059**[2] **(**EpCAMx4-1BB) Multiple solid tumors	**Autogene cevumeran (BNT122)**[1] 1L adv. melanoma, + pembrolizumab	
BNT221 Refractory metastatic melanoma	**BNT315/GEN1055**[2] (OX40) Multiple solid tumors	**Autogene cevumeran (BNT122)**[1] Adj. ctDNA+ stage II or III CRC	
BNT321 (sLea) Metastatic PDAC	**BNT316/ONC-392 (gotistobart)**[4] (CTLA-4) mCRPC, + radiotherapy	**Autogene cevumeran (BNT122)**[1] Adj. PDAC, + atezolizumab + mFOLFIRINOX	
BNT322/GEN1056[2] Multiple solid tumors	**BNT316/ONC-392 (gotistobart)**[4] (CTLA-4) Multiple solid tumors	**BNT311/GEN1046 (acasunlimab)**[2] (PD-L1x4-1BB) R/R met. NSCLC, +/- pembrolizumab	
BNT326/YL202[3] (HER3) Multiple solid tumors	**BNT321** (sLeA) adjuvant PDAC, +mFOLFIRINOX	**BNT316/ONC-392 (gotistobart)**[4] (CTLA-4) Plat.-R. ovarian cancer, + pembrolizumab	
	BNT323/DB-1303[5] (HER2) Multiple solid tumors	**BNT327/PM8002**[7] (PD-L1 x VEGF-A) 1L/2L+ ES-SCLC, +chemotherapy	
	BNT324/DB-1311[5] (B7H3) Multiple solid tumors	**BNT327/PM8002**[7] (PD-L1 x VEGF-A) 1L/2L met. TNBC, +chemotherapy	
	BNT325/DB-1305[5] (TROP2) Multiple solid tumors		
	BNT327 / BNT325 combination[7,5] Multiple solid tumors		

Legend

- mRNA
- Cell therapy
- Next generation IO
- ADCs
- Novel combination studies

1. Partnered with Genentech, member of Roche Group; 2. Partnered with Genmab; 3. Partnered with MediLink Therapeutics; 4.Partnered with OncoC4; 5. Partnered with DualityBio; 6. Trials jointly conducted with Regeneron; 7. Partnered with Biotheus. Molecules are investigational and have not been approved as safe and effective for use by any regulatory authority, including the U.S. FDA.

BIONTECH

BioNTech at ESMO 2024 (1/2)

Modality	Program	Type Code	Title	Date, Time & Location
mRNA therapeutic vaccines	**BNT113**	Poster 877P	Exploratory efficacy and translational results from the safety run in of AHEAD-MERIT, a phase II trial of first line pembrolizumab plus the fixed-antigen cancer vaccine BNT113 in advanced HPV16+ HNSCC	• Sat, 14.09.2024 • Hall 6
	BNT113	Mini-oral 27LO	HARE-40: A phase I/II trial of therapeutic HPV vaccine (BNT113) in patients with HPV16 driven carcinoma	• Mon, 16.09.2024 • 11:15 - 11:20 AM CEST • Granada Auditorium - Hall 6
Cell therapies	**BNT211**	Proffered paper (10 min presentation) 611O	BNT211-01 (NCT04503278), an ongoing, first-in-human, Phase 1 study evaluating safety and efficacy of CLDN6 CAR T cells and a CLDN6-encoding mRNA vaccine in patients with relapsed/refractory CLDN6+ solid tumors	• Sun, 15.09.2024 • 15:45 - 15:55 PM CEST • Salamanca Auditorium - Hall 5

BioNTech at ESMO 2024 (2/2)

Modality	Program	Type Code	Title	Date, Time & Location
Protein-based Therapeutics	**BNT323 / DB-1303[1]**	TiP 436TiP	DYNASTY-Breast02: A Phase 3 trial of BNT323/DB-1303 vs investigator's choice chemotherapy in HER2-low, hormone receptor positive, metastatic breast cancer	• Mon, 16.09.24 • Granada Auditorium - Hall 6
	BNT314 / GEN1059[2]	TiP 1072TiP	Phase 1/2 dose escalation/expansion trial to evaluate safety and preliminary efficacy of DuoBody-EpCAMx4-1BB (BNT314/GEN1059) alone or in combination with an immune checkpoint inhibitor in patients with malignant solid tumors	• Sat, 14.09.2024 • Granada Auditorium - Hall 6
	BNT316 / ONC-392[3]	LBA LBA32	A randomized, Phase 2, dose optimization of gotistobart, a pH-sensitive anti-CTLA-4, in combination with standard dose pembrolizumab in platinum-resistant recurrent ovarian cancer: safety, efficacy and dose optimization (PRESERVE-004/GOG-3081)	• Sun, 15.09.24 • 08:30 – 10:00 AM CEST • Burgos Auditorium – Hall 5
	BNT327 / PM8002[4]	Mini-oral 1255MO	A Phase II safety and efficacy study of PM8002/BNT327 in combination with chemotherapy in patients with EGFR-mutated non-small cell lung cancer (NSCLC)	• Sat, 14.09.2024 • 10:25 - 10:30 AM CEST • Santander Auditorium - Hall 5
	BNT327 / PM8002[4]	Mini-oral 348MO	A Phase Ib/II study to assess the safety and efficacy of PM8002/BNT327 in combination with nab-paclitaxel for first line treatment of locally advanced or metastatic triple-negative breast cancer	• Mon, 16.09.2024 • 08:35 - 08:40 AM CEST • Barcelona Auditorium - Hall 2
	BNT327 / PM8002[4]	Poster 1692P	A Phase Ib/IIa trial to evaluate the safety and efficacy of PM8002/ BNT327, a bispecific antibody targeting PD-L1 and VEGF-A, as a monotherapy in patients with advanced renal cell carcinoma	• Sun, 15.09.2024 • Granada Auditorium - Hall 6

Partnered with: 1. DualityBio; 2. Genentech, member of Roche Group; 3. OncoC4; 4. Biotheus.

BIONTECH

1

1 BNT327 / PM8002[1]

EGFR-mutated Non-Small Cell Lung Cancer

A Phase II Safety and Efficacy Study of PM8002/BNT327 in Combination with Chemotherapy in Patients with EGFR-mutated Non-Small Cell Lung Cancer (NSCLC)

Yi-Long Wu, MD, (Lung Cancer Institute, Guangdong Province People's Hospital, Guangzhou, China) et al., Presentation Number: 1255MO

1. Partnered with Biotheus Inc.

BIONTECH

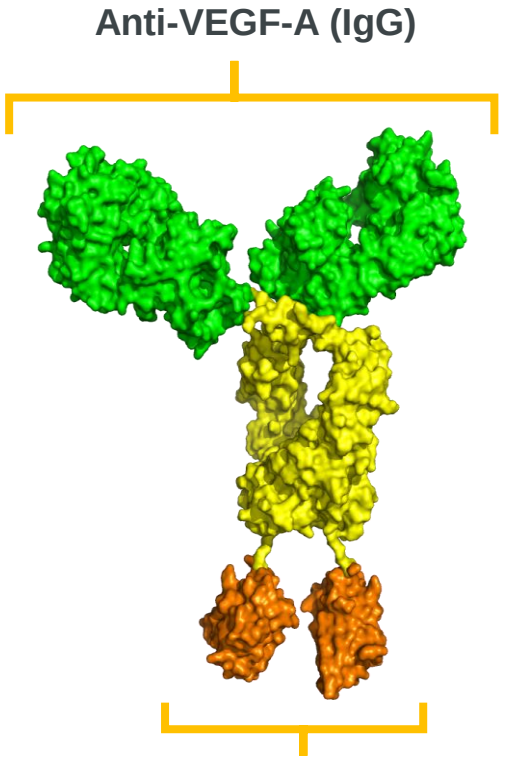
BNT327/PM8002[1] – A Next-Gen IO Agent that Combines Two Clinically Validated MoAs

Dual blockade of PD-L1 and VEGF-A has demonstrated clinical synergy

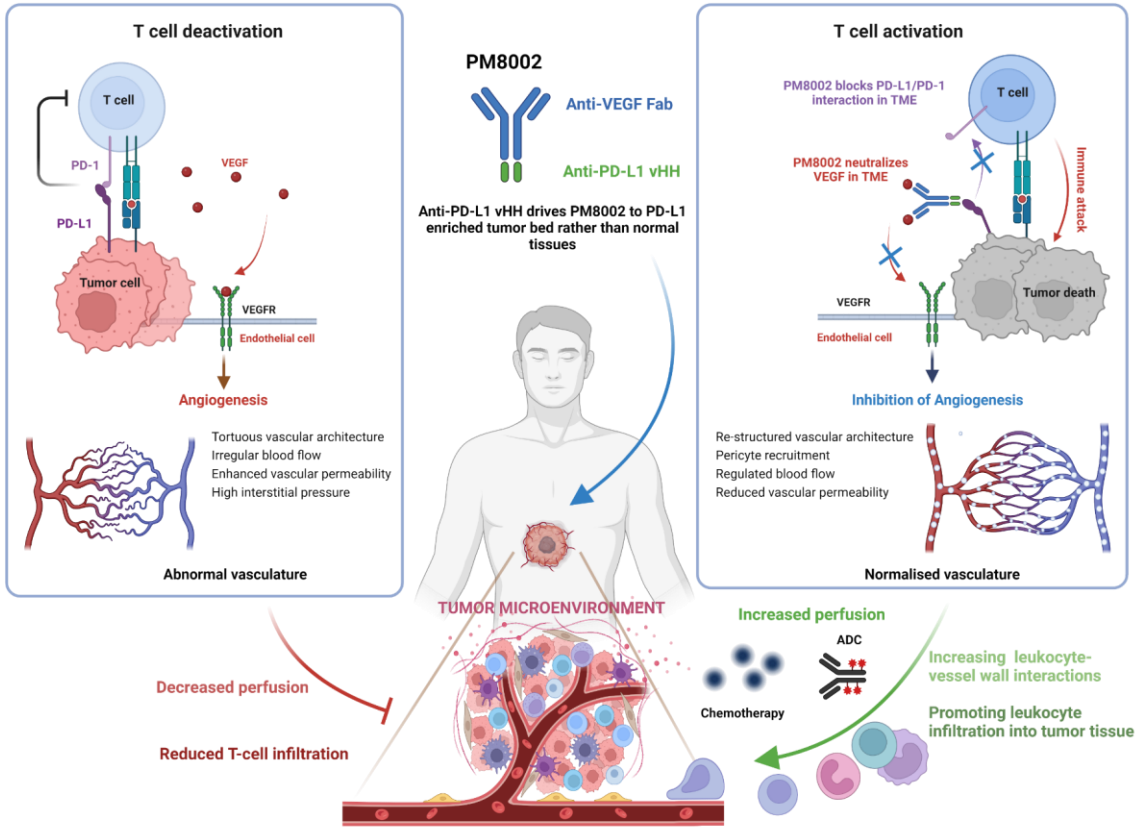
- Compelling profile with over 600 patients treated to date
- Monotherapy activity and synergy in combination therapy observed in early clinical studies
- Encouraging safety profile vs. PD-L1 + VEGF inhibition or PD-1 alone

Protein binding activity (K_D) for human

- PD-L1: 5.5 nM
- VEGF-A: <0.4 nM



"Two in one" mechanism-of-action synergizes with ADCs



1. Partnered with Biotheus Inc. ADC = antibody drug conjugate; IgG = immunoglobulin G; IO = immuno-oncology; MoA = Mechanism of Action; PD-1 = programmed cell death protein 1; PD-L1 = programmed cell death ligand 1; TME = tumor microenvironment; VEGF = vascular endothelial growth factor; VHH = heavy chain variable. The mechanism of action graphic was generated by Biorender.com.

BNT327/PM8002[1] in Combination with Chemotherapy in Patients with Advanced NSCLC

Multicenter, single arm, Phase 2 study to evaluate efficacy and safety of BNT327/PM8002 in combination with chemotherapy in patients with advanced NSCLC (NCT05756972)

Inclusion criteria

- Age ≥ 18 years
- Nonsquamous Stage IIIB/C and IV NSCLC ineligible for surgery or local therapy
- EGFR sensitizing mutation
- Failure of EGFR-TKI treatment(s)
- No other prior systemic therapy than EGFR-TKIs
- Asymptomatic/stable brain metastasis allowed

N=64

BNT327/PM8002[1], 30 mg/kg +
Carboplatin, AUC 5 mg/ml/min +
Pemetrexed, 500 mg/m^2
Q3W for 4 cycles

BNT327/PM8002[1], 30 mg/kg +
Pemetrexed, 500 mg/m^2
Maintenance Q3W

Endpoints

Primary: ORR (assessed by investigator per RECIST 1.1)

1. Partnered with Biotheus, Inc.

CTx = chemotherapy; ECOG = Eastern Cooperative Oncology Group; mEGFR = mutated epidermal growth factor receptor; NSCLC = non-small cell lung cancer; ORR = objective response rate; QxW = every x weeks; RECIST = Response Evaluation Criteria in Solid Tumors; SoC = standard of care; TKI = tyrosine kinase inhibitor.

Baseline Characteristics

	Overall n=64	PD-L1 negative (TPS＜1%) n=28	PD-L1 low expression (TPS 1 to 49%) n=23	PD-L1 high expression (TPS ≥ 50%) n=13
Median age, years (range)	59.5 (32,76)	59.0 (36,76)	59.6 (44,75)	60.2 (32,74)
Female, n (%)	29 (45.3)	11 (39.3)	11 (47.8)	7 (53.8)
Brain metastasis, n (%)	15 (23.4)	7 (25.0)	5 (21.7)	3 (23.1)
Liver metastasis, n (%)	11 (17.2)	5 (17.9)	5 (21.7)	1 (7.7)
EGFR mutation, n (%)				
19Del	32 (50.0)	10 (35.7)	15 (65.2)	7 (53.8)
L858R	29 (45.3)	17 (60.7)	7 (30.4)	5 (38.5)
Others*	3 (4.7)	1 (3.6)	1 (4.4)	1 (7.7)
T790M status, n (%)				
Negative	39 (60.9)	19 (67.9)	15 (65.2)	5 (38.5)
Positive	12 (18.8)	6 (21.4)	4 (17.4)	2 (15.4)
Unknown	13 (20.3)	3 (10.7)	4 (17.4)	6 (46.2)
Previous EGFR-TKI treatment, n (%)				
1st/2nd Gen TKI only	5 (7.8)	3 (10.7)	0 (0)	2 (15.4)
3rd Gen TKI only	41 (64.1)	17 (60.7)	16 (69.6)	8 (61.5)
1st/2nd Gen TKI, then 3rd Gen TKI	18 (28.1)	8 (28.6)	7 (30.4)	3 (23.1)

*others: S768I, L861Q, G719X

Analysis by PD-L1 expression was determined with immunohistochemistry and classified based on tumor proportion score (TPS). All biopsies were taken after progression on EGFR-TKI therapy.

Cut-off date: July 24, 2024

1. Partnered with Biotheus, Inc.

EGFR = epidermal growth factor receptor; Gen = generation; TKI = tyrosine kinase inhibitor;

BNT327/PM8002[1] Showed Anti-Tumor Activity Independent of PD-L1 Expression Levels

Response Assessment	Overall n=64	PD-L1 negative n=28	PD-L1 low expression n=23	PD-L1 high expression n=13
ORR by investigator, n (%) [95% CI]	39 (60.9) [47.9, 72.9]	13 (46.4) [27.5, 66.1]	14 (60.9) [38.5, 80.3]	12 (92.3) [64.0, 99.8]
Confirmed ORR by investigator, n (%) [95% CI]	37 (57.8) [44.8, 70.0]	11 (39.3) [21.5, 59.4]	14 (60.9) [38.5, 80.3]	12 (92.3) [64.0, 99.8]
Best overall response, n (%)				
PR	37 (57.8)	11 (39.3)	14 (60.9)	12 (92.3)
SD	24 (37.5)	15 (53.6)	9 (39.1)	0 (0)
PD	3 (4.7)	2 (7.1)	0 (0)	1 (7.7)
DCR, n (%) [95% CI]	61 (95.3) [86.9, 99.0]	26 (92.9) [76.5, 99.1]	23 (100) [85.2, 100.0]	12 (92.3) [64.0, 99.8]
Median TTR, months [95% CI]	2.9 [1.5, 4.1]	5.8 [2.7, NE]	2.9 [1.4, NE]	1.6 [1.5, 2.9]

Analysis by PD-L1 expression was determined with immunohistochemistry and classified based on tumor proportion score (TPS). All biopsies were taken after progression on EGFR-TKI therapy.

Cut-off date: July 24, 2024
Median follow-up time: 7.7 months

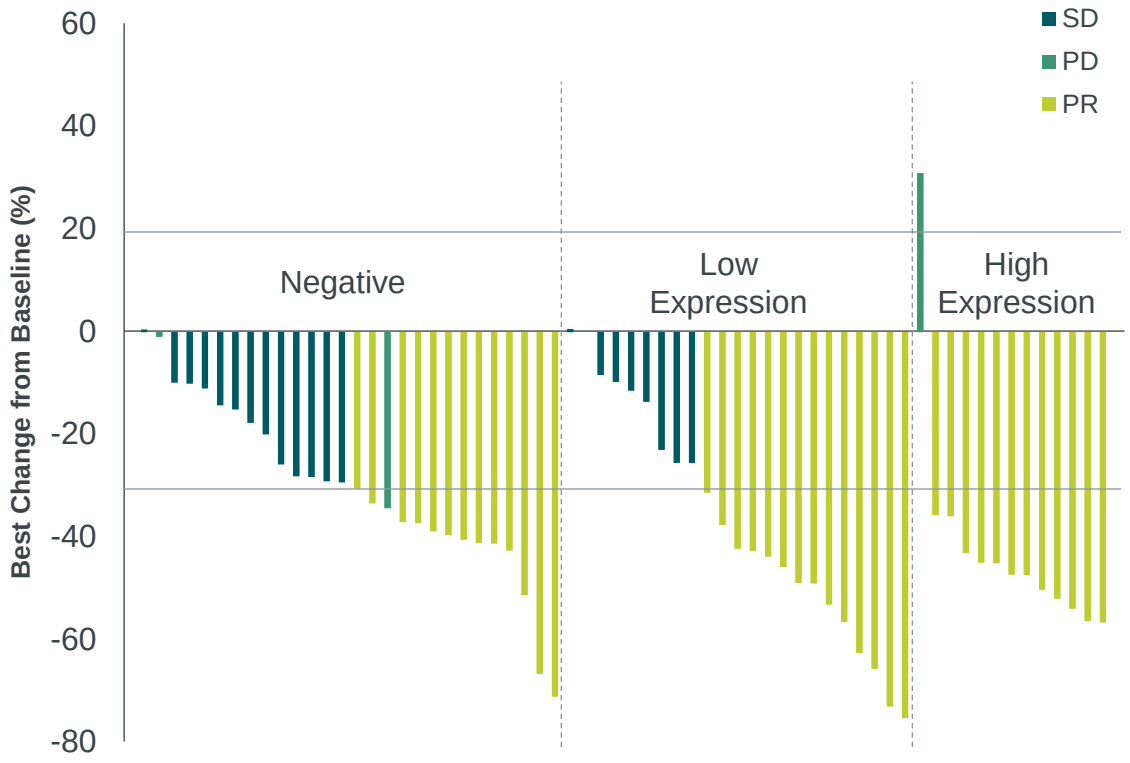
1. Partnered with Biotheus Inc.

CI = confidence interval; DCR = disease control rate; NE = not evaluable.; ORR = objective response rate; PD = progressive disease; PD-L1 = programmed cell death ligand 1; PR = partial response; SD = stable disease; TTR = time to response.

ESMO 2024 | Yi-Long Wu, et. al., Phase II Study of BNT327/PM8002 in EGFR-mutated NSCLC, (NCT05756972), Presentation 1255MO

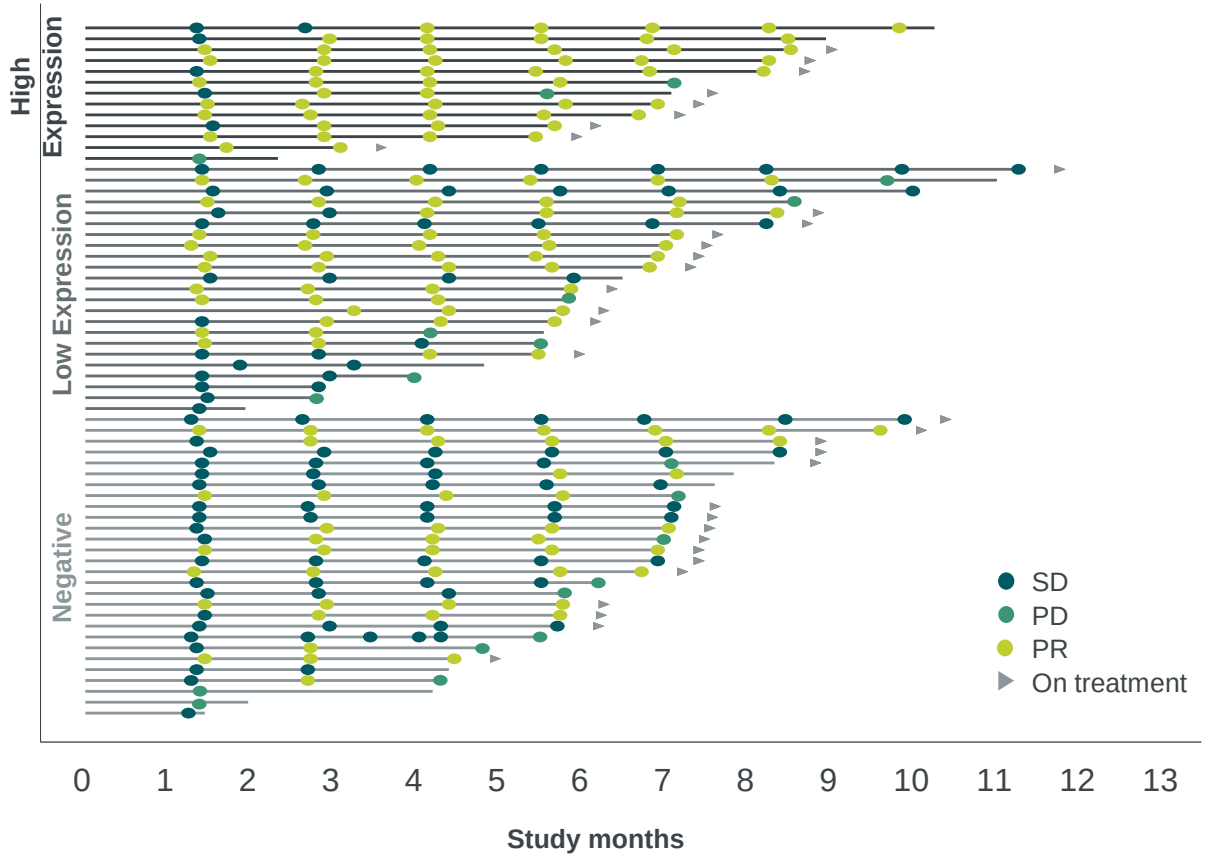
BNT327/PM8002[1] Showed Positive Correlation Between Higher Tumor PD-L1 Expression Levels and Overall Response Rates

Waterfall plot of best change of target lesions from baseline for patients grouped by PD-L1 expression



Median follow-up time: 7.7 months

Swimmer plot of treatment duration for patients grouped by PD-L1 expression



1. Partnered with Biotheus Inc.,
PD = progressive disease; PD-L1 = programmed cell death ligand 1; PR = partial response; SD = stable disease.

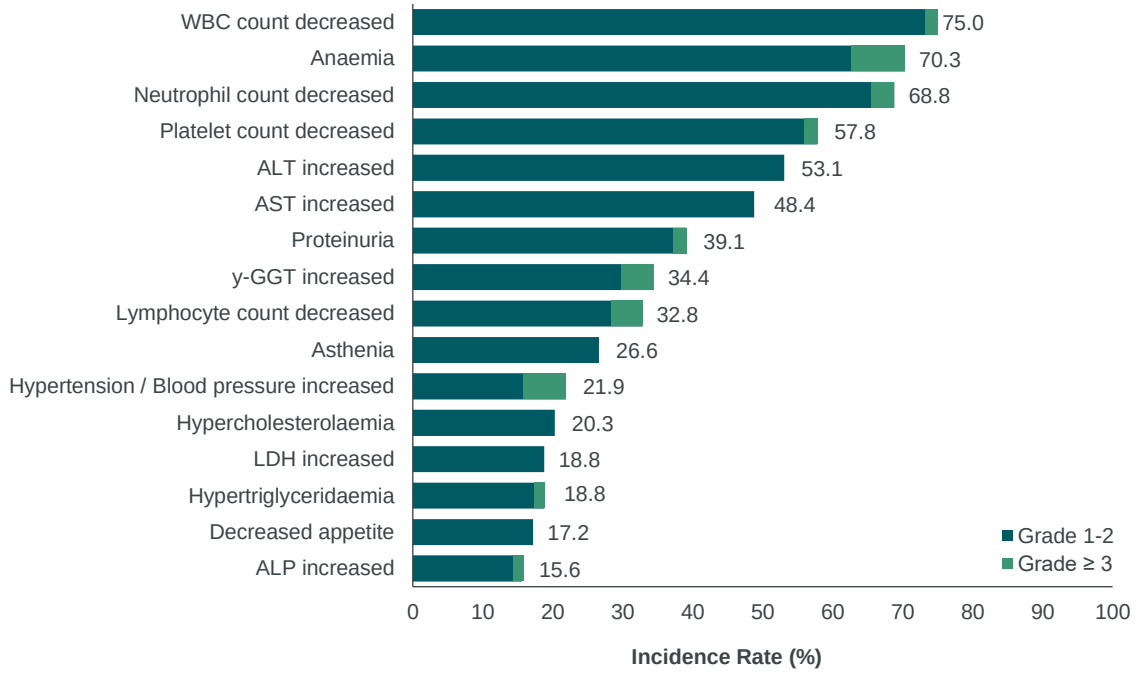
BIONTECH

BNT327/PM8002[1] Shows Generally Manageable Safety Profile

Safety summary

	Overall (n=64)
Any TEAE, n (%)	64 (100)
Grade ≥3	45 (70.3)
Any TRAE, n (%)	63 (98.4)
Grade ≥3	39 (60.9)
Leading to interruption of PM8002/BNT327	20 (31.3)
Leading to discontinuation of only PM8002/BNT327	4 (6.3)
Leading to discontinuation of only chemotherapy	4 (6.3)
Leading to discontinuation of PM8002/BNT327 and chemotherapy	1 (1.6)
Leading to death#	1 (1.6)
Any-grade immune-related	26 (40.6)
Grade ≥3 immune-related	4 (6.3)
Grade ≥3 VEGF-related*	7 (10.9)
SAE	11 (17.2)

TRAEs occurring in ≥ 15% of patients



#TRAE leading to death: 1 case of pneumonia.
**Grade ≥3 VEGF-related TRAEs included hypertension/elevated blood pressure, proteinuria, epistaxis, hemoptysis.*

Cut-off date: July 24, 2024
Median follow-up time: 7.7 months

Only low rate of treatment discontinuation due to TRAEs

1. Partnered with Biotheus Inc; ALP = Alkaline phosphatase.; ALT = Alanine aminotransferase; AST = Aspartate aminotransferase; LDH, Lactate dehydrogenase; SAE = serious adverse event (related to any drug); TEAE = treatment-emergent adverse event; TRAE = treatment-related adverse event (related to any drug); WBC = White blood cell; γ-GGT = Gamma-glutamyltransferase;.

ESMO 2024 | Yi-Long Wu, et. al., Phase II Study of BNT327/PM8002 in EGFR-mutated NSCLC, (NCT05756972), Presentation 1255MO

BIONTECH

BNT327/PM8002[1] (EGFRmut NSCLC) – ESMO 2024 Data: Key Takeaway Messages

Efficacy

BNT327PM8002[1] plus chemotherapy showed encouraging antitumor activity in patients with EGFR-mutated NSCLC who progressed on prior EGFR-TKI treatment(s).

The anti-tumor activity of BNT327/PM8002[1] therapy was observed independent of PD-L1 expression levels (PD-L1 negative NSCLC showed 39.3% cORR), with a positive correlation seen between higher tumor PD-L1 expression levels and overall response rates.

Safety Profile

The safety profile was generally manageable, with a low rate of treatment discontinuation.

Outlook

Based on these findings, further clinical trials in NSCLC are warranted.

1. Partnered with Biotheus Inc.; EGFRmut = mutated epidermal growth factor receptor; NSCLC = non-small cell lung cancer; cORR = confirmed objective response rate; PD-L1 = programmed cell death ligand 1.

ESMO 2024 | Yi-Long Wu, et. al., Phase II Study of BNT327/PM8002 in EGFR-mutated NSCLC, (NCT05756972), Presentation 1255MO

1

2

BNT327 / PM8002[1]

Metastatic Triple-Negative Breast Cancer

A Phase Ib/II Study to Assess the Safety and Efficacy of PM8002/BNT327 in Combination with Nab-Paclitaxel for First Line Treatment of Locally Advanced or Metastatic Triple-Negative Breast Cancer

Dr. Yanchun Meng (Fudan University Shanghai Cancer Center, Shanghai, China) et al., Presentation Number: 348MO

1. Partnered with Biotheus Inc.

BIONTECH

BNT327/PM8002[1] in Combination with Nab-Paclitaxel as First Line Treatment for Patients with Metastatic TNBC

Phase Ib/II open-label, single-arm study to evaluate safety and efficacy of BNT327/PM8002 in combination with nab-paclitaxel as 1L treatment in advanced or metastatic TNBC (NCT05918133)

Inclusion criteria

- Age 18-75 years with life expectancy ≥ 12 weeks
- Histologically or cytologically confirmed unresectable adv. or met. ER, PR, HER-2 negative TNBC
- No prior systemic therapy despite taxane in (neo)adj. settings, ≥ 12 months
- ≥ 1 measurable lesion (RECIST 1.1)
- ECOG PS 0-1
- Adequate organ function

N=60

BNT327/PM8002,
20 mg/kg
On days: 1 and 15 (Q2W) of 28-day cycle

+

Nab-paclitaxel
100 mg/m^2
On days 1, 8 and 15 of 28-day cycle

Treatment continued
until disease progression
or unacceptable toxicity

Key endpoints

Primary	ORR (RECIST1.1), safety (NCI-CTCAE v5.0)
Secondary	PFS, DCR, OS

1. Partnered with Biotheus, Inc. ; 1L = first line; DCR = disease control rate; DOR = durability of response; ECOG PS= eastern cooperative oncology group performance status; ER = estrogen receptor; HER-2 = human epidermal growth factor receptor 2; NCI-CTCAE = National Cancer Institute Common Terminology Criteria for Adverse Events; ORR = Overall response rate; OS = overall survival; PFS = progression free survival; PR = progesterone receptor; Q2W = every two weeks; RECIST = Response Evaluation Criteria in Solid Tumors; TNBC = triple-negative breast cancer; TRAEs = treatment-related adverse events.

ESMO 2024 | Y. Meng, et. al., Phase Ib/II Study of BNT327/PM8002 with Nab-Paclitaxel as 1L in mTNBC, (NCT05918133), Presentation 348MO

Baseline Characteristics

Study status

As of July 05, 2024, **42 patients had been enrolled** and received at least 1 dose of BNT327/ PM8002 combined with nab-paclitaxel

11 pts remained on treatment

Median follow-up time 16.3 months

Patient Characteristics (n=42)	
Median age, years (Q1, Q3)	53.5 (41.0, 60.0)
Number of metastatic sites, n (%)	
0-2	17 (40.5)
≥ 3	25 (59.5)
Liver metastasis, n (%)	
Yes	16 (38.1)
No	26 (61.9)
Brain metastasis, n (%)	
Yes	2 (4.8)
No	40 (95.2)
Neo/adjuvant Paclitaxel treatment, n (%)	
Yes	28 (66.7)
No	14 (33.3)

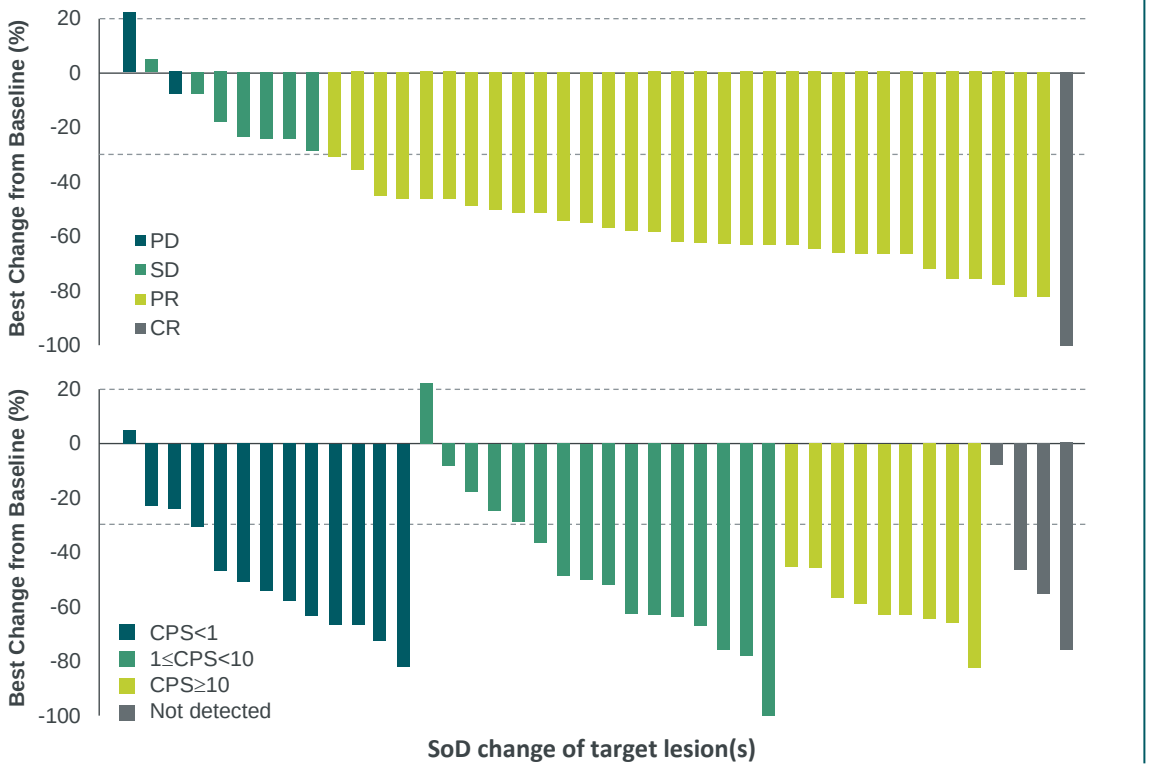
Partnered with Biotheus Inc.;
irAEs = immune-related adverse events; SAEs = severe adverse events; TNBC = triple-negative breast cancer; TRAEs = treatment-related adverse events.

ESMO 2024 | Y. Meng, et. al., Phase Ib/II Study of BNT327/PM8002 with Nab-Paclitaxel as 1L in mTNBC, (NCT05918133), Presentation 348MO

BNT327/PM8002[1] Showed Clinically Meaningful Efficacy irrespective of PD-L1 status

Variable	ITT	PD-L1 CPS<1	PD-L1 1≤CPS<10	PD-L1 CPS≥10	Not detected
Population (n)	42	13	16	9	4
CR	1 (2.4)	0 (0.0)	1 (6.3)	0 (0.0)	0 (0.0)
PR	32 (76.2)	10 (76.9)	10 (62.5)	9 (100.0)	3 (75.0)
SD	7 (16.7)	3 (23.1)	4 (25.0)	0 (0.0)	0 (0.0)
PD	2 (4.8)	0 (0.0)	1 (6.3)	0 (0.0)	1 (25.0)
ORR % (95% CI)	78.6 (63.2, 89.7)	76.9 (46.2, 95.0)	68.8 (41.3, 89.0)	100.0 (66.4, 100.0)	75.0 (19.4, 99.4)
cORR % (95% CI)	73.8 (58.0, 86.1)	76.9 (46.2, 95.0)	56.3 (29.9, 80.3)	100.0 (66.4, 100.0)	75.0 (19.4, 99.4)
DCR % (95% CI)	95.2 (83.8, 99.4)	100.0 (75.3, 100.0)	93.8 (69.8, 99.8)	100.0 (66.4, 100.0)	75.0 (19.4, 99.4)
mPFS (Mo), (95%CI)	13.5 (9.4, --)	NR (5.7, --)	14.0 (7.2, --)	10.8 (5.5, 13.5)	14.0 (1.8, --)

For the ITT population, mTTR was 1.9 mo and mDoR 11.7 mo; mOS was not reached



PD-L1 status was assessed by means of the PD-L1 IHC E1L3N assay

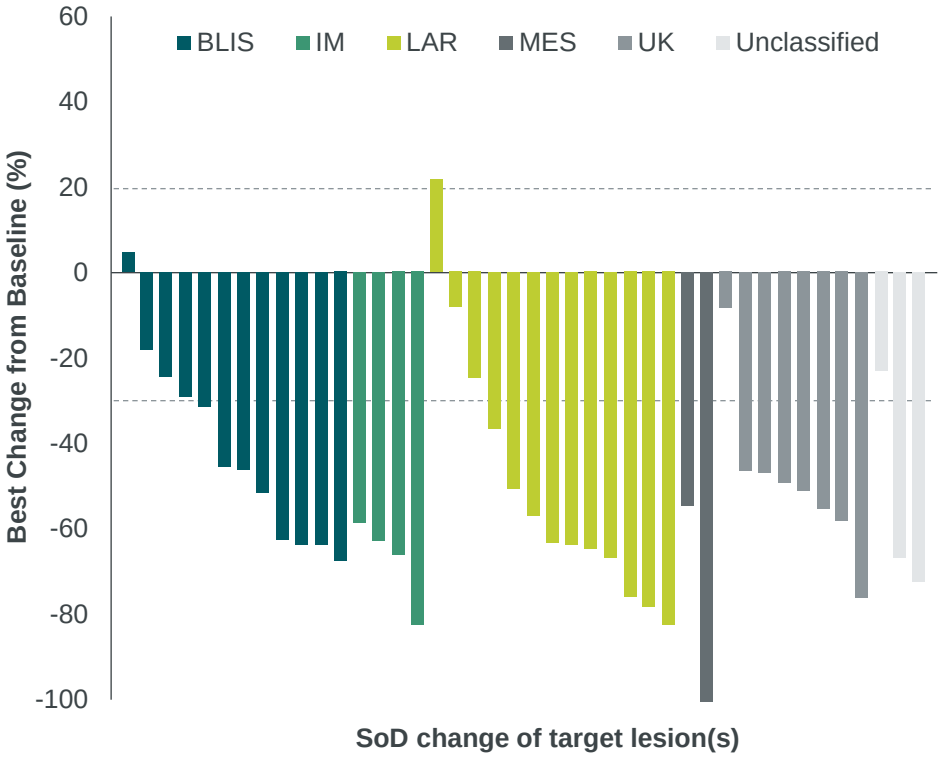
1. Partnered with Biotheus Inc.;
CPS = combined positive score; CR = complete response; cORR = confirmed ORR; DCR = disease control rate; IHC = immunohistochemistry; ITT = intention to treat; mDoR = median duration of response; mOS = median overall survival; mPFS = median progress-free survival; mTTR = median time to response; ORR = objective response rate; PD = progressive disease; PD-L1 = programmed cell death ligand 1; PR = partial response; SD = stable disease; SoD = sum of diameters

ESMO 2024 | Y. Meng, et. al., Phase Ib/II Study of BNT327/PM8002 with Nab-Paclitaxel as 1L in mTNBC, (NCT05918133), Presentation 348MO

BIONTECH

BNT327/PM8002[1] Showed Similar ORR Regardless of FUDAN Type

Variable	BLIS	IM	LAR	MES	Unclassified	Unknown
Population (n)	12	4	13	2	3	8
CR	0 (0.0)	0 (0.0)	0 (0.0)	1 (50.0)	0 (0.0)	0 (0.0)
PR	8 (66.7)	4 (100.0)	10 (76.9)	1 (50.0)	2 (66.7)	7 (87.5)
SD	4 (33.3)	0 (0.0)	2 (15.4)	0 (0.0)	1 (33.3)	0 (0.0)
PD	0 (0.0)	0 (0.0)	1 (7.7)	0 (0.0)	0 (0.0)	1 (12.5)
ORR, % (95% CI)	66.7 (34.9, 90.1)	100.0 (39.8, 100.0)	76.9 (46.2, 95.0)	100.0 (15.8, 100.0)	66.7 (9.4, 99.2)	87.5 (47.3, 99.7)
cORR, % (95% CI)	58.3 (27.7, 84.8)	100.0 (39.8, 100.0)	69.2 (38.6, 90.9)	100.0 (15.8, 100.0)	66.7 (9.4, 99.2)	87.5 (47.3, 99.7)
DCR % (95% CI)	100.0 (73.5, 100.0)	100.0 (39.8, 100.0)	92.3 (64.0, 99.8)	100.0 (15.8, 100.0)	100.0 (29.2, 100.0)	87.5 (47.3, 99.7)



1. Partnered with Biotheus Inc.;
BLIS = basal-like and immune-suppressed; CR = complete response; cORR = confirmed ORR; DCR = disease control rate; FUDAN Type = molecular subtype classification determined by IHC analysis, developed by Fudan University Shanghai Cancer Center; IM = immunomodulatory; LAR = luminal androgen receptor; mDoR = median duration of response; MES = mesenchymal-like; mPFS = median progress-free survival; mTTR = median time to response; ORR = objective response rate; PD = progressive disease; PR = partial response; SD = stable disease; SoD = sum of diameters; UK = unknown

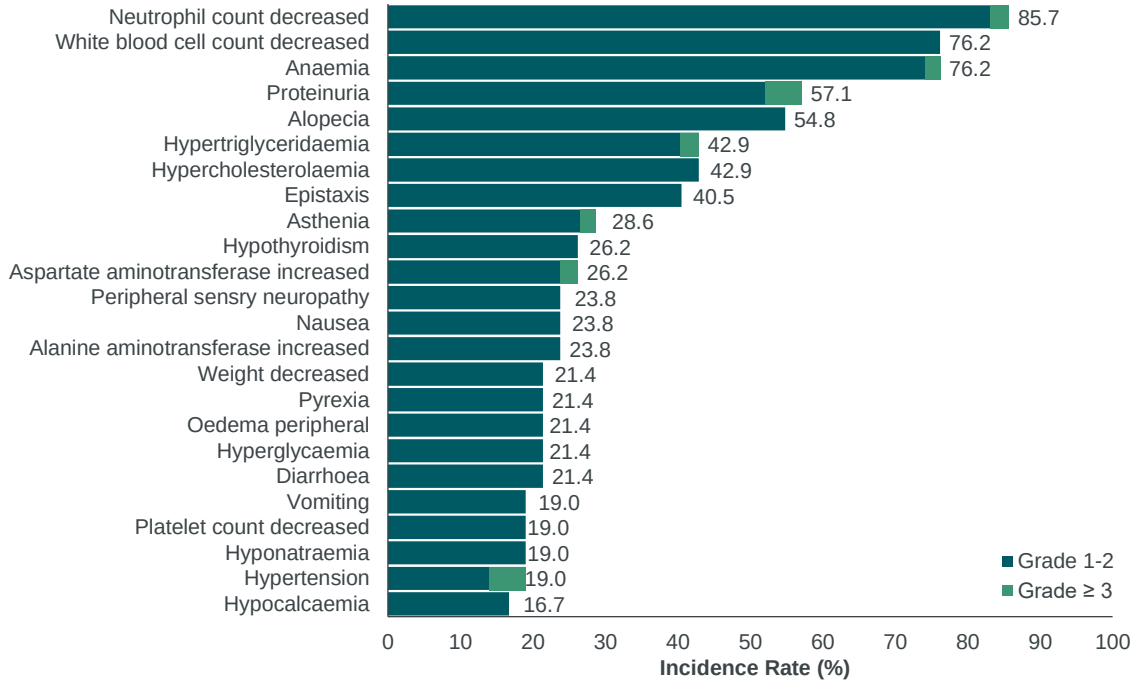
ESMO 2024 | Y. Meng, et. al., Phase Ib/II Study of BNT327/PM8002 with Nab-Paclitaxel as 1L in mTNBC, (NCT05918133), Presentation 348MO

BNT327/PM8002[1] - Safety Profile in Patients with TNBC

Safety summary

Safety Overview	N=42 n (%)
All TRAEs	42 (100)
Grade ≥3 TRAEs	24 (57.1)
SAEs	10 (23.8)
TRAE leading to dose interruption	27 (64.3)
TRAE leading to dose reduction	7 (16.7)
TRAEs leading to treatment discontinuation	2 (4.8)
irAE	15 (35.7)
Grade ≥3 irAE	4 (9.5)

TRAEs occurring in ≥ 15% of patients



Any-grade and grade ≥3 TRAEs of the combination regimen occurred in 100% and 57.1% patients, respectively TRAEs leading to treatment discontinuation occurred in 4.8% patients

1. Partnered with Biotheus Inc.; irAEs = immune-related adverse events; SAEs = severe adverse events; TNBC = triple-negative breast cancer; TRAEs = treatment-related adverse events.

ESMO 2024 | Y. Meng, et. al., Phase Ib/II Study of BNT327/PM8002 with Nab-Paclitaxel as 1L in mTNBC, (NCT05918133), Presentation 348MO

BIONTECH

BNT327/PM8002[1] (mTNBC) – ESMO 2024 Data: Key Takeaway Messages

Efficacy

In patients with locally advanced/metastatic TNBC, first line treatment with BNT327/PM8002[1] + nab-paclitaxel is associated with:

- Rapid shrinkage of target lesions.
- Clinically meaningful antitumor activity regardless of PD-L1 status and FUDAN type.

Safety Profile

Manageable toxicity: No new safety signals were observed beyond those typically described for anti-PD-1/PD-L1 and anti-VEGF therapies and chemotherapy.

Outlook

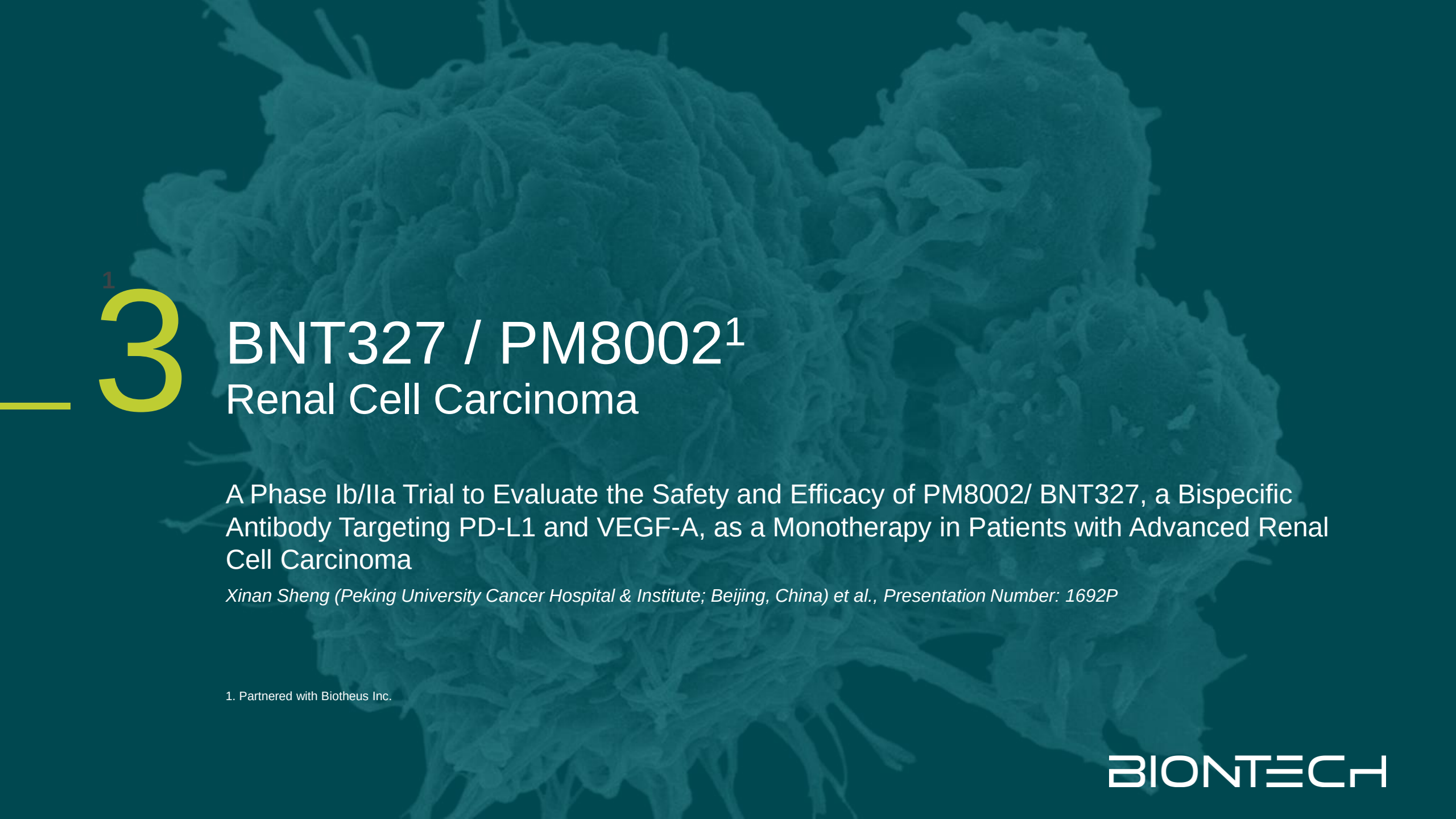
Study limitations: single arm and small sample size.

BNT327/PM8002[1] shows a favorable safety profile and early signals of efficacy in first line treatment of TNBC which will be further explored in ongoing trials.

Phase III trial (NCT06419621) in China as well as global Phase II trial (NCT06449222) ongoing in TNBC.

1. Partnered with Biotheus Inc.;
FUDAN Type = molecular subtype classification determined by IHC analysis, developed by Fudan University Shanghai Cancer Center; mTNBC = metastatic triple negative breast cancer; PD-(L)1 = programmed cell death protein (ligand) 1; VEGF = vascular epidermal growth factor;

ESMO 2024 | Y. Meng, et. al., Phase Ib/II Study of BNT327/PM8002 with Nab-Paclitaxel as 1L in mTNBC, (NCT05918133), Presentation 348MO



3[1]

BNT327 / PM8002[1]

Renal Cell Carcinoma

A Phase Ib/IIa Trial to Evaluate the Safety and Efficacy of PM8002/ BNT327, a Bispecific Antibody Targeting PD-L1 and VEGF-A, as a Monotherapy in Patients with Advanced Renal Cell Carcinoma

Xinan Sheng (Peking University Cancer Hospital & Institute; Beijing, China) et al., Presentation Number: 1692P

1. Partnered with Biotheus Inc.

BIONTECH

Trial Design of BNT327/PM8002[1] Monotherapy in Patients with Advanced Solid Tumors including 2L ccRCC and 1L nccRCC

Phase 1b/2a open-label multiple cohort, dose-expansion monotherapy study to evaluate safety and efficacy of BNT327/PM8002 in patients with advanced solid tumors, including RCC (NCT05918445)

Inclusion criteria

- Age 18-75 years with life expectancy ≥ 12 weeks
- Locally advanced inoperable or metastatic RCC with or without sarcomatoid component
  - ccRCC: progress on prior 1L VEGF TKI +/- IO
  - nccRCC: no prior systemic therapy
- Malignant tumor confirmed by histology or cytology
- Adequate organ function
- ≥ 1 measurable lesion not been previously treated (RECIST 1.1)
- ECOG 0-1

N = 53 →

BNT327/PM8002, iv,
Q2W or Q3W

Treatment continued until disease progression or intolerable toxicity

Study endpoints

Primary: ORR assessed by investigators per RECIST v1.1

Secondary: DCR (RECIST v1.1), DOR (RECIST v1.1), PFS, safety

1. Partnered with Biotheus Inc.; ccRCC = clear cell renal cell carcinoma DCR = disease control rate; DOR = duration of response; ECOG = Eastern Cooperative Oncology Group; iv = intravenously; nccRCC = non-clear cell renal cell carcinoma,; ORR = objective response rate; PFS = progression free survival; PK = pharmacokinetic parameters, QxW = every x weeks; RECIST = Response Evaluation Criteria in Solid Tumors;

ESMO 2024 | Xinan Sheng, et. al., Phase Ib/IIa trial with BNT327/PM8002 as a monotherapy in adv. RCC, (NCT05918445), Presentation 1692P

BNT327/PM8002[1] Phase 1b/2a Study in Patients with RCC – Baseline Characteristics

Study status

As of July 5, 2024, **31 patients with ccRCC** and **22 patients with nccRCC** had been enrolled.

A few patients had favorable-risk disease in both cohorts and majority of patients had intermediate or poor risk score.

In the nccRCC cohort, the most common histologic subtype was papillary.

Median duration of follow-up was 14.1 months (0.9, 27.6) in ccRCC and 9.0 months (1.6, 26.9) in nccRCC.

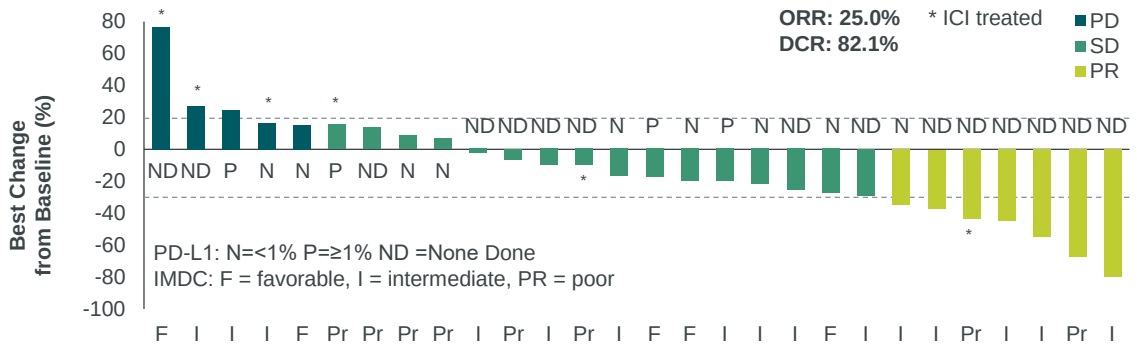
Characteristics	2L ccRCC (n=31)	1L nccRCC (n=22)
Median age, years (Q1, Q3)	59.0 (54.0, 66.0)	53.5 (42.0, 62.0)
Sex, n (%)		
Male	20 (64.5)	16 (72.7)
Female	11 (35.5)	6 (27.3)
ECOG, n (%)		
0	12 (38.7)	10 (45.5)
1	19 (61.3)	12 (54.5)
IMDC risk group, n (%)		
Favorable	6 (19.4)	2 (9.1)
Intermediate/poor	25 (80.6)	20 (90.9)
PD-L1 CPS, n (%)		
＜1%	9 (29.0)	3 (13.6)
≥1%	5 (16.1)	1 (4.6)
Not Done	17 (54.8)	18 (81.8)
Histology, n (%)		
Clear cell	31 (100)	0
Papillary	0	10 (45.5)
TFE3	0	4 (18.2)
FH-deficient	0	3 (13.6)
Other*	0	5 (22.7)
Prior systemic anticancer therapy, n (%)		
VEGF TKI only	25 (80.6)	0
VEGF TKI and prior ICIs	6 (19.4)	0
Previous nephrectomy, n (%)	21 (67.7)	15 (68.2)

1. Partnered with Biotheus Inc.; *Other included ESC RCC (n=2), translocation RCC (n=1), oncocytoma (n=1) and chromophobe (n=1).
CPS = combined positive score; ECOG = Eastern Cooperative Oncology Group; FH = Fumarate hydratase; ICI = immune checkpoint inhibitor; IMDC = International Metastatic Renal Cell Carcinoma Database Consortium; (n)ccRCC = (non-) clear cell renal cell carcinoma; PD-L1 = programmed cell death ligand 1; TFE3 = RCC = renal cell carcinoma; VEGF TKI = Vascular endothelial growth factor tyrosine kinase inhibitors.

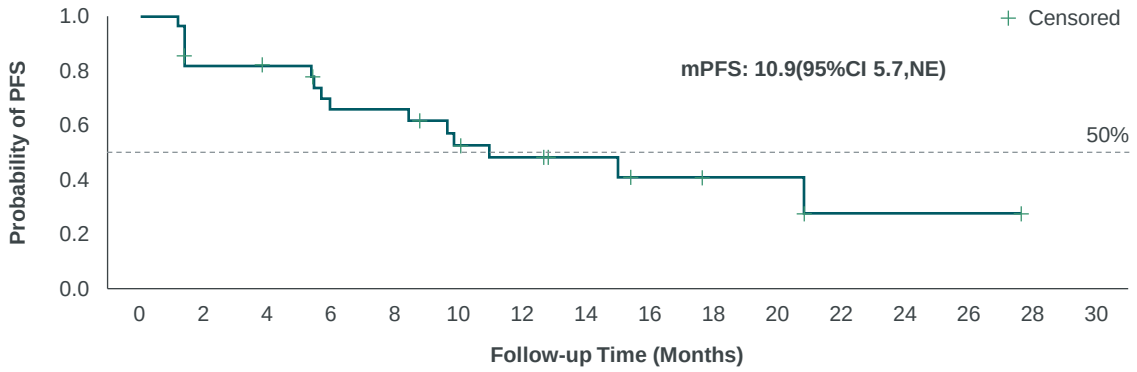
ESMO 2024 | Xinan Sheng, et. al., Phase Ib/IIa trial with BNT327/PM8002 as a monotherapy in adv. RCC, (NCT05918445), Presentation 1692P

BNT327/PM8002[1] Showed Encouraging Anti-Tumor Activity in Patients with ccRCC (n = 28)

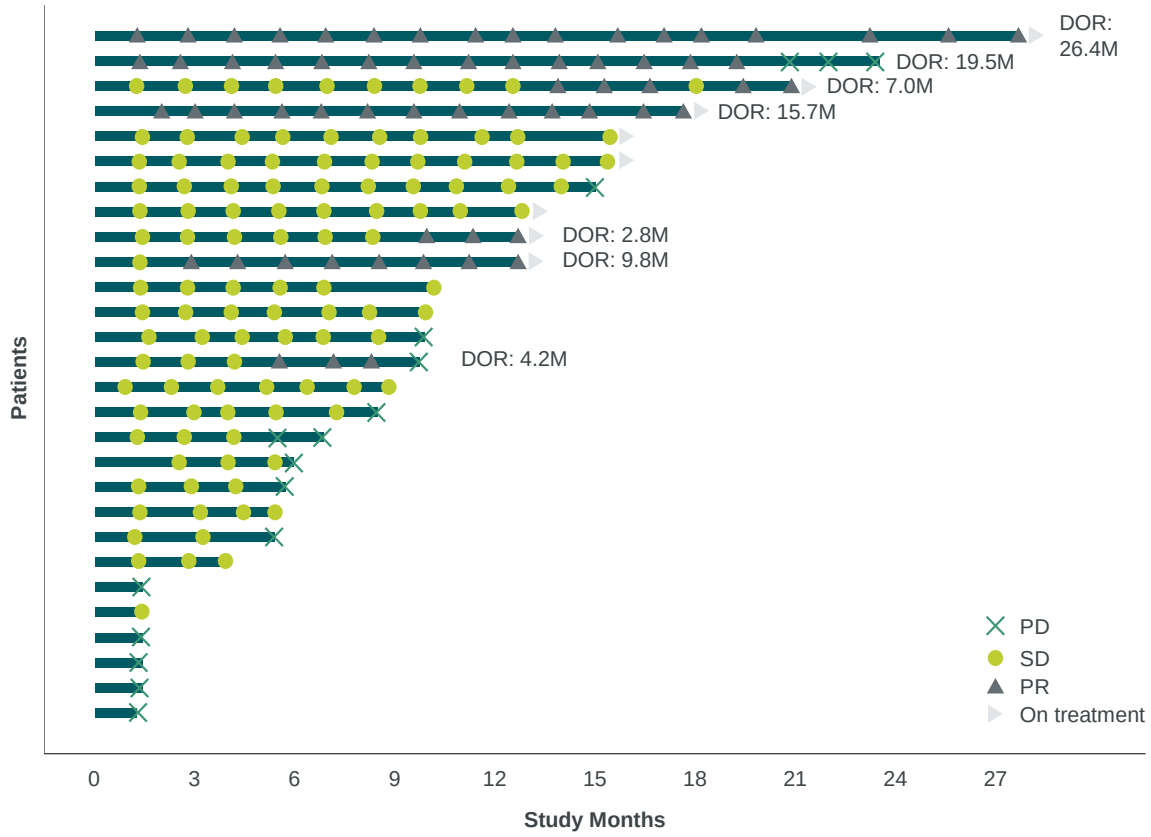
ORR: 25.0%; DCR: 82.1%



mPFS: 10.9 months (95%CI: 5.7, NE)



mDOR: 19.6 months (95%CI: 4.2, NE)



1. Partnered with Biotheus Inc.

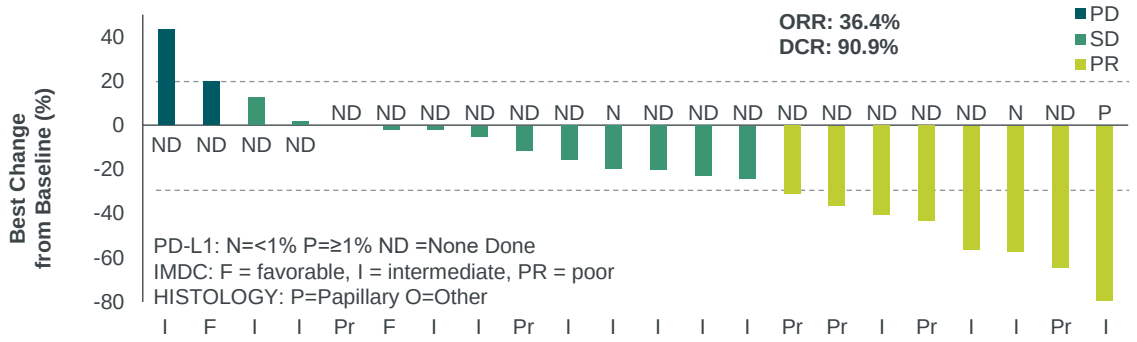
ccRCC = clear cell renal cell carcinoma; CI = confidence interval; DCR = disease control rate; DOR = duration of response; ICI = immune checkpoint inhibitor; IMDC = International Metastatic Renal Cell Carcinoma Database Consortium; mPFS = median progression free survival; ORR = overall response rate; PD = progressive disease; PR = partial response; SD = stable disease; NE = not evaluable.

ESMO 2024 | Xinan Sheng, et. al., Phase Ib/IIa trial with BNT327/PM8002 as a monotherapy in adv. RCC, (NCT05918445), Presentation 1692P

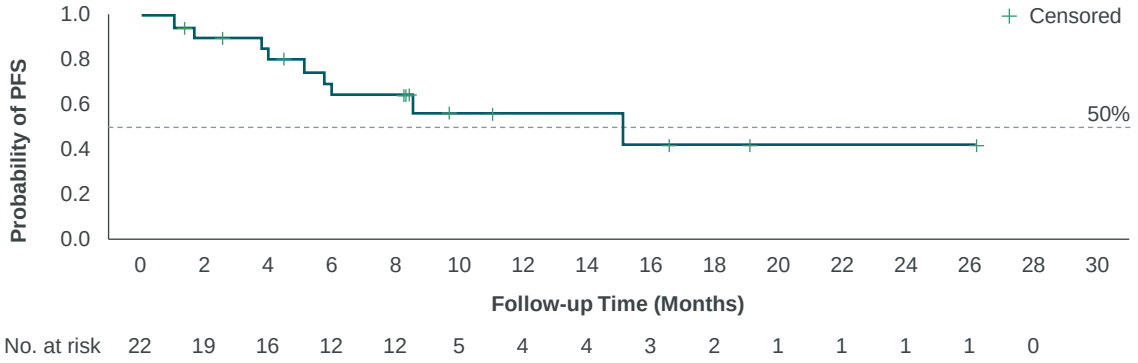
BIONTECH

BNT327/PM8002[1] Showed Encouraging Anti-Tumor Activity in Patients with nccRCC across subtypes (n = 22)

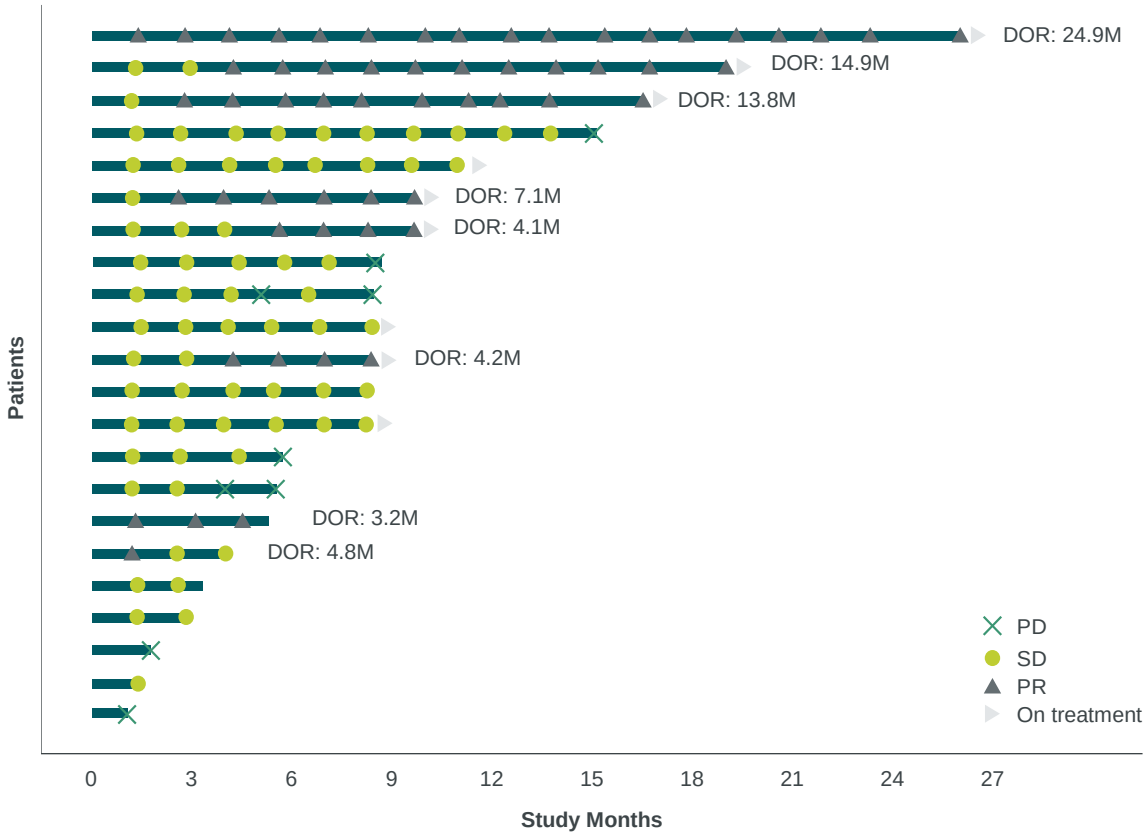
ORR: 36.4%; DCR: 90.9%



mPFS: 15.1 months (95%CI: 5.7, NE)



DOR of up to 24.9 months



1. Partnered with Biotheus Inc.;
CI = confidence interval; DCR = disease control rate; DOR = duration of response; IMDC = International Metastatic Renal Cell Carcinoma Database Consortium; mPFS = median progression free survival; nccRCC = non-clear cell renal cell carcinoma; ORR = overall response rate; PD = progressive disease; PR = partial response; SD = stable disease; NE = not evaluable.

ESMO 2024 | Xinan Sheng, et. al., Phase Ib/IIa trial with BNT327/PM8002 as a monotherapy in adv. RCC, (NCT05918445), Presentation 1692P

BIONTECH

BNT327/PM8002[1] - Safety in Patients with Advanced nccRCC or ccRCC

Safety observations

All patients experienced any-grade treatment-related adverse events (TRAEs).

Most AEs were Grades 1-2.

Categories	n (%)
All TRAEs	53 (100)
≥Grade 3 TRAEs	22 (41.5)
irAEs	26 (49.1)
SAEs	8 (15.1)
TRAEs leading to discontinuation	1 (1.9)

		Grade, n (%)		
TRAE ≥10%	All	3	4	5
Proteinuria	30 (56.6)	8 (15.1)	0	0
Hypertriglyceridaemia	16 (30.2)	2 (3.8)	0	0
Hypercholesterolaemia	15 (28.3)	0	0	0
Hypertension	11 (20.8)	8 (15.1)	0	0
Blood creatinine increased	10 (18.9)	0	0	0
Blood pressure increased	9 (17.0)	3 (5.7)	0	0
Low density lipoprotein increased	9 (17.0)	0	0	0
Apolipoprotein B increased	9 (17.0)	0	0	0
Blood cholesterol increased	8 (15.1)	0	0	0
Rash	8 (15.1)	0	0	0
Hypoalbuminaemia	8 (15.1)	0	0	0
Anaemia	8 (15.1)	0	0	0
Alanine aminotransferase increased	7 (13.2)	0	0	0
Gamma-glutamyltransferase increased	6 (11.3)	0	0	0
Blood thyroid stimulating hormone increased	6 (11.3)	0	0	0
Hypothyroidism	6 (11.3)	0	0	0
Blood creatine phosphokinase increased	6 (11.3)	0	0	0
Hyperuricaemia	6 (11.3)	0	0	0

1. Partnered with Biotheus Inc.:
irAEs = immune related adverse events; (n)ccRCC = (non-)clear cell renal cell carcinoma; SAEs = serious adverse events; TRAEs = treatment related adverse events;

ESMO 2024 | Xinan Sheng, et. al., Phase Ib/IIa trial with BNT327/PM8002 as a monotherapy in adv. RCC, (NCT05918445), Presentation 1692P

BNT327/PM8002[1] (RCC) – ESMO 2024 Data: Key Takeaway Messages

Efficacy:

BNT327/PM8002[1] showed encouraging anti-tumor activity:

ccRCC Cohort (n = 28 evaluable patients)

- ORR was 25.0% with 7 confirmed PR, 16 SD, and 5 PD, DCR was 82.1%
- mPFS was 10.9 months (95% CI: 5.7, NE), mDoR 19.6 months (95% CI: 4.2, NE)

nccRCC Cohort (n = 22 evaluable patients)

- ORR was 36.4% with 8 PR (7 confirmed) and 12 SD, DCR was 90.9%.
- mPFS was 15.1 months (95% CI: 5.7,NE).
- Responses were observed across subtypes of nccRCC. The highest ORR (60%) was among patients with papillary.

Safety Profile:

BNT327/PM8002[1] showed manageable safety in patients with previously untreated advanced nccRCC or advanced ccRCC after failure of the combination of anti-PD-1/L1 and VEGF-TKI therapy or VEGF-TKI monotherapy.

Outlook:

Further clinical development in RCC is warranted.

1. Partnered with Biotheus Inc.;

CI = confidence interval; DCR = disease control rate; DOR = duration of response; IMDC = International Metastatic Renal Cell Carcinoma Database Consortium; mPFS = median progression free survival; (n)ccRCC = (non-)clear cell renal cell carcinoma; NE = not evaluable; ORR = overall response rate; PD = progressive disease; PD-L1 = programmed cell death ligand 1; PR = partial response; SD = stable disease; VEGF TKI = Vascular endothelial growth factor tyrosine kinase inhibitors.

ESMO 2024 | Xinan Sheng, et. al., Phase Ib/IIa trial with BNT327/PM8002 as a monotherapy in adv. RCC, (NCT05918445), Presentation 1692P

1

4 BNT316 / ONC-392[1]

Platinum-Resistant Ovarian Cancer

PRESERVE-004/GOG-3081 (NCT05446298):

A Phase 2 randomized dose optimization trial of gotistobart, a pH-sensitive anti-CTLA-4, in combination with pembrolizumab in platinum-resistant ovarian cancer

Joyce N. Barlin (Women's Cancer Care Associates, Albany, NY, United States) et al., Presentation Number: LBA32

1. Partnered with OncoC4

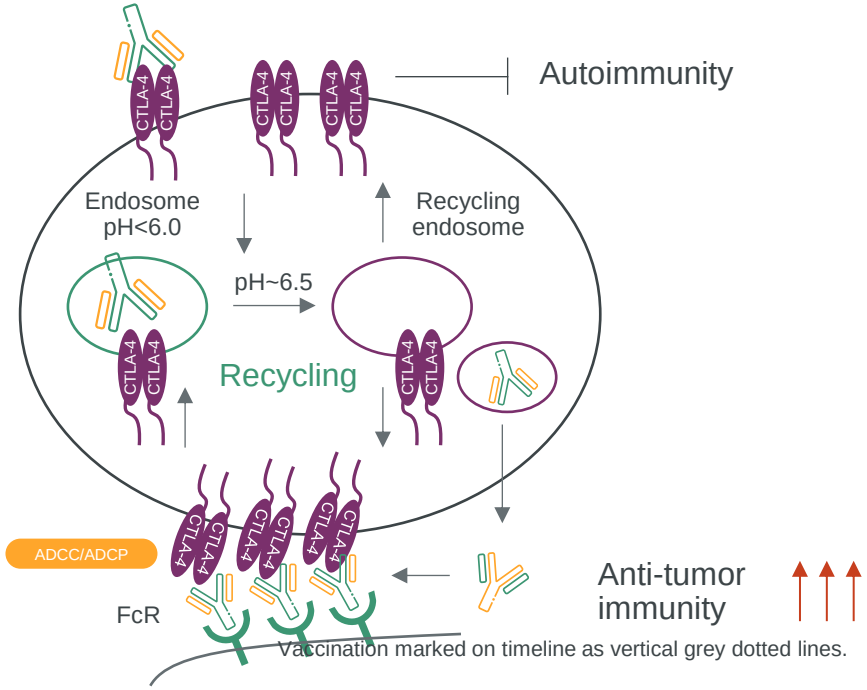
BIONTECH

BNT316/ONC-392 (Gotistobart)[1] is a pH-sensitive CTLA-4-preserving Antibody

Avoiding lysosomal degradation of CTLA-4 for safer and more effective immunotherapy may lead to uncoupling cancer therapeutic effect from immunotherapy-related adverse effects

BNT316/ONC-392 (gotistobart)[1] designed to:

- Allow regular recycling and enrichment of antibody and CTLA-4 molecule
- Enhance anti-tumor immunity
- Reduce immune-related adverse events



MoA designed to allow higher dosing & longer duration of treatment with BNT316/ONC-392 (gotistobart)[1]

Liu Y. et al. Abstract # 231, SITC 2021. Du et al. Uncoupling therapeutic from immunotherapy-related adverse effects for safer and effective anti-CTLA-4 antibodies in CTLA4 humanized mice. Cell Res. 2018 Apr; 28(4): 416–432. Du et al. A reappraisal of CTLA-4 checkpoint blockade in cancer immunotherapy. Cell Res. 2018 Apr; 28(4): 433–447.

1.Partnered with OncoC4. ADCC = antibody-dependent cell-mediated cytotoxicity, ADCP = antibody-dependent cellular phagocytosis; CTLA-4 = cytotoxic T-lymphocyte-associated protein 4, FcR = fragment crystallizable region.

ESMO 2024 | Joyce N. Barlin, et. al., Phase 2 trial of BNT316/ONC-392 in platinum-resistant ovarian cancer (NCT05446298), Presentation LBA32

BIONTECH

BNT316/ONC-392 (Gotistobart)[1] in Combination with Pembrolizumab in Patients with Platinum-Resistant Ovarian Cancer (PRESERVE-004)

Phase 2 randomized, open-label, multicenter study to evaluate safety and efficacy of BNT316/ONC-392 (gotistobart)[1] in combination with pembrolizumab in patients with PROC (NCT05446298)

Inclusion criteria

- Age ≥ 18 years
- Prior SoC of surgical intervention, including hysterectomy and salpingo-oophorectomy
- Resistant to platinum-based CTx and disease progression on therapy containing bevacizumab
- More than 1 prior systemic lines of anti-cancer therapy
- Measurable lesions (RECIST 1.1)
- ECOG score 0-1

N=21, R 1:1

- **BNT316/ONC-392 (gotistobart)[1],** 3 mg/kg,iv **+ pembrolizumab,** 200 mg, iv, Q3W
- **BNT316/ONC-392 (gotistobart)[1],** 6 mg/kg, iv **+ pembrolizumab,** 200 mg iv, Q3W

Dose reduction recommended after study initiation

N=62, R 1:1

- **BNT316/ONC-392 (gotistobart)[1],** 1 mg/kg, iv, Q3W **+ pembrolizumab,** 200 mg, iv, Q3W (N = 33)
- **BNT316/ONC-392 (gotistobart)[1],** 2 mg/kg, iv, Q3W **+ pembrolizumab,** 200 mg iv, Q3W (N=29)

Treatment continued until confirmed CD, PD, toxicity, withdrawal, or completion of 35 treatment cycles

Key endpoints

Primary:	ORR (by INV per RECIST 1.1), irAEs, TRAEs, TRSAEs
Secondary:	DoR, DCR, BoR, PFS, OS
Exploratory:	PK, ER, TRAE-related study discontinuation

1. Partnered with OncoC4

BOR = best overall response; CTx = chemotherapy; DCR = disease control rate; DOR = duration of response; ECOG = Eastern Cooperative Oncology Group; irAEs = immune-related adverse events; ORR = objective response rate; OS = overall survival; PK/PD = pharmacokinetics/pharmacodynamics; PARP = poly (ADP-ribose) polymerase; PFS = progression-free survival; PROC = platinum-resistant ovarian cancer; Q3W = every three weeks; RECIST = Response Evaluation Criteria in Solid Tumors; SoC = standard of care; TRAEs = treatment-related adverse events.

ESMO 2024 | Joyce N. Barlin, et. al., Phase 2 trial of BNT316/ONC-392 in platinum-resistant ovarian cancer (NCT05446298), Presentation LBA32

PRESERVE-004: Baseline Disease Characteristics and Study Drug Exposure

	BNT316/ONC-392 (gotistobart)[1] + pembrolizumab 200mg	
Characteristic	**1 mg/kg (n = 33)**	**2 mg/kg (n = 29)**
Age – median (range), years	65.2 (10.25)	63.5 (8.46)
Race – n (%)		
White/ Black/ Asian/ Other	27 (81.8)/ 1 (3.0)/ 1 (3.0)/ 3 (9.1)	25 (86.2)/ 2 (6.9)/ 1 (3.4)/ 1 (3.4)
ECOG performance-status score – n (%)		
0	19 (57.6)	15 (51.7)
1	14 (42.4)	14 (48.3)
Primary cancer diagnosis n (%)		
High-grade serous ovarian cancer	28 (84.8)	25 (86.2)
Primary peritoneal cancer	3 (9.1)	2 (6.9)
Fallopian tube cancer	2 (6.1)	2 (6.9)
Metastatic disease at enrolment, n (%)	24 (72.7)	25 (86.2)
Prior cancer regimens – median (range)	4.0 (2–9)	3.0 (1–8)
BEV-naïve, n (%)	6 (18.2)	12 (41.4)
Study drug exposure		
Treatment duration, mean months (SD)	3.03 (2.43)	3.18 (2.45)
Gotistobart cycles, median (range)	3.0 (1–12)	3.0 (1–12)
Gotistobart dose intensity, % (range)	98.4 (56.6–106.9)	98.4 (56.7–105.1)

Data cut-off: July 19, 2024.

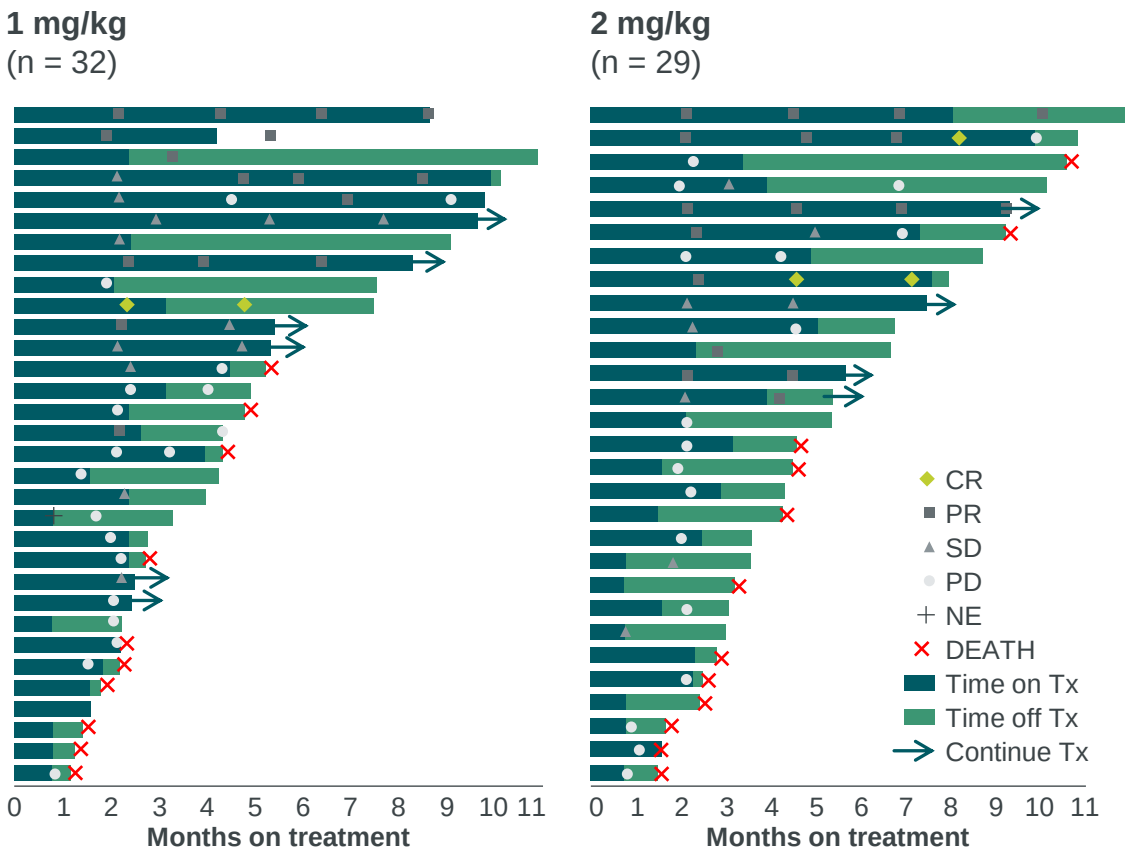
1. Partnered with OncoC4;
BEV = Bevacizumab; ECOG = Eastern Cooperative Oncology Group; SD = standard deviation.

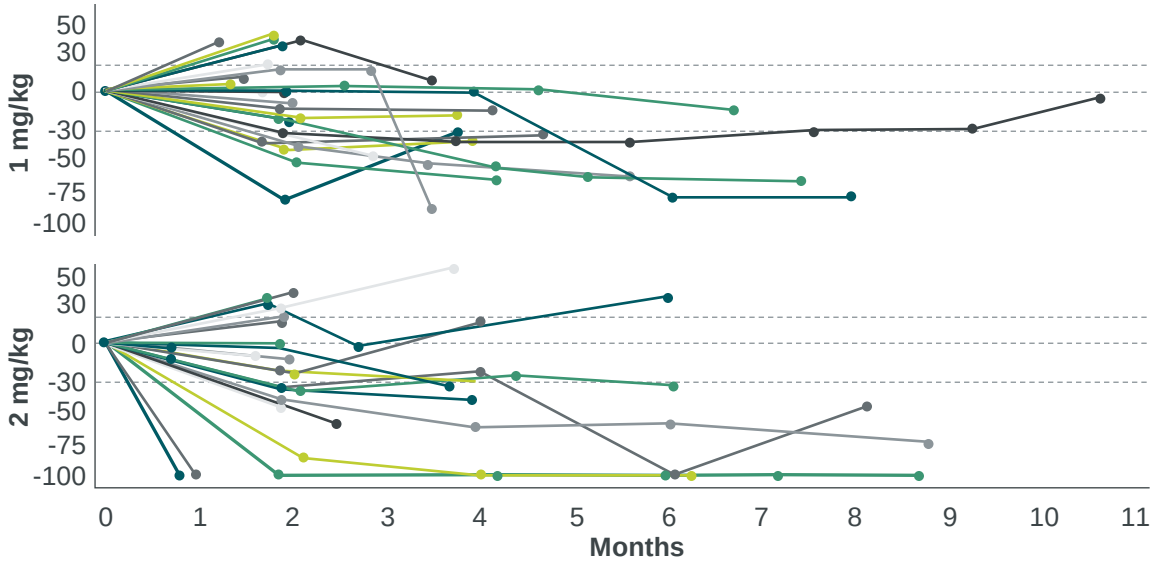
ESMO 2024 | Joyce N. Barlin, et. al., Phase 2 trial of BNT316/ONC-392 in platinum-resistant ovarian cancer (NCT05446298), Presentation LBA32

BIONTECH

BNT316/ONC-392 (Gotistobart)[1] Plus Pembrolizumab Showed Encouraging Preliminary Efficacy

BNT316/ONC-392 (gotistobart)[1] + pembrolizumab 200mg





	BNT316/ONC-392 (gotistobart)[1] + pembrolizumab 200mg	
	1 mg/kg (N=32)	2 mg/kg (N=29)
ORR (unconfirmed) % (n) 95% CI	**25.0% (8)** 11.5 – 43.4	**27.6% (8)** 12.7 – 47.2
Complete response[a,b]	3.1% (1)	6.9% (2)
Partial response[a]	21.9% (7)	20.7% (6)
Stable disease	21.9% (7)	13.8% (4)
Progressive disease	40.6% (13)	44.8% (13)
No post-baseline assessment[c]	12.5% (4)	13.8% (4)

Data cut-off: July 19, 2024.

1.Partnered with OncoC4; a. Includes both confirmed and unconfirmed responses (3 unconfirmed responders in each treatment group); b. One out of 3 unconfirmed responders are still on treatment, for both treatment groups; c. Patients died or discontinued from study without any post-baseline scan. CR = complete response; ORR = objective response rate; PD = progressive disease; PR = partial response; SD = stable disease.

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BNT316/ONC-392 (Gotistobart)[1] - Tolerability Profile at Both Dose Levels

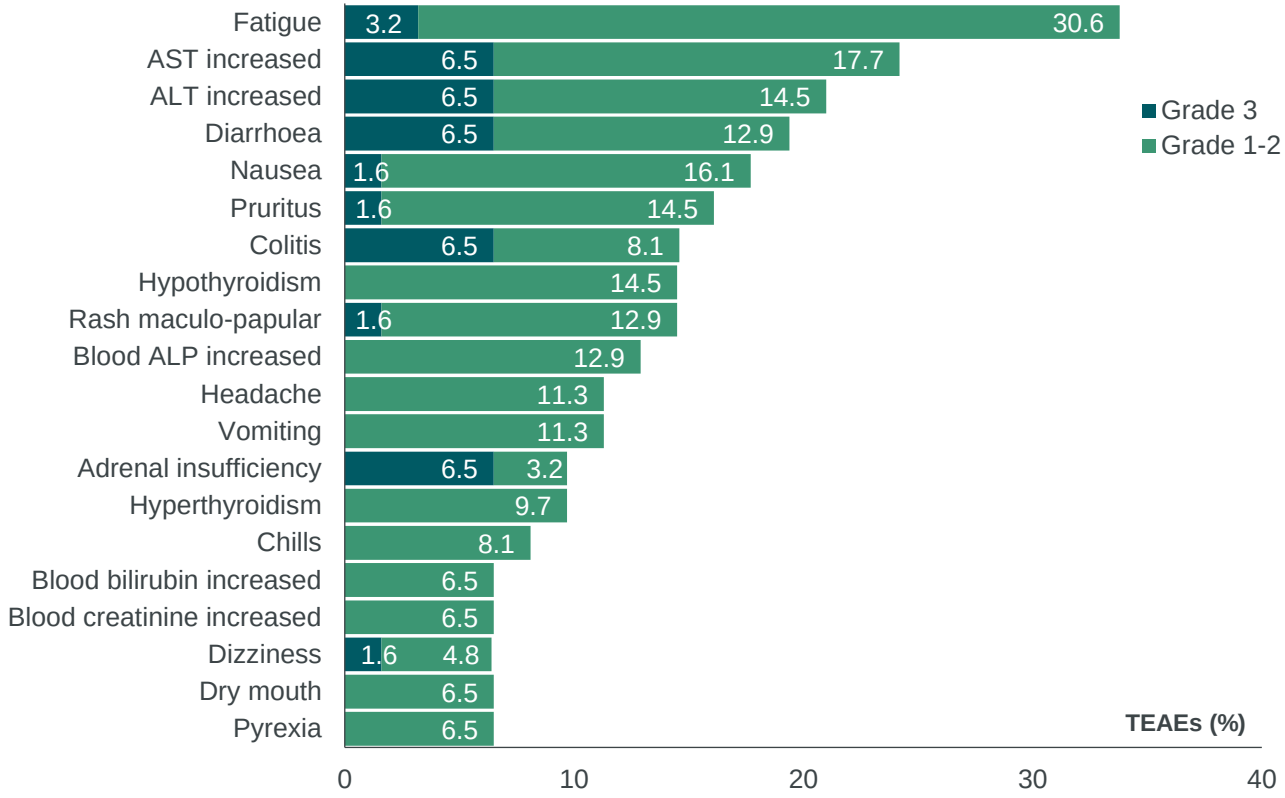
Safety summary

	Gotistobart[1] + pembrolizumab 200 mg	
	1 mg/kg N = 33	2 mg/kg N = 29
TEAEs, n (%)	33 (100.0)	28 (96.6)
Grade ≥ 3, n (%)	25 (75.8)	25 (86.2)
TEAEs related to either drug, n (%)	27 (81.8)	23 (79.3)
Grade ≥ 3, n (%)	15 (45.5)	12 (41.4)
Serious TEAEs	18 (54.5)	21 (72.4)
irAE All grades, n (%)	15 (45.5)	18 (62.1)
Grade ≥ 3, n (%)	8 (24.2)	11 (37.9)
TEAEs leading to gotistobart discontinuation	7 (21.2)	8 (27.6)

Data cut-off: July 19, 2024.

TEAEs occurring mostly Grade 1-2

Most common TEAEs related to either drug (≥5 % in combined 1 mg and 2 mg groups)



1.Partnered with OncoC4;
ALP = alkaline phosphatase; ALT = alanine transaminase; AST = aspartate aminotransferase; irAE = immune-related adverse event; SD = standard deviation ; TEAE = treatment emergent adverse event.

ESMO 2024 | Joyce N. Barlin, et. al., Phase 2 trial of BNT316/ONC-392 in platinum-resistant ovarian cancer (NCT05446298), Presentation LBA32

Gotistobart[1] – ESMO 2024 Data: Key Takeaway Messages

Efficacy

Preliminary results for efficacy are encouraging

The final dose selection will be based on the totality of safety, efficacy, and pharmacology

Safety Profile

Early results from PRESERVE-004 demonstrate that gotistobart + pembrolizumab in PROC has a manageable tolerability profile at both dose levels, with no new safety signals

Outlook

If confirmed by further preplanned analyses, the combination of gotistobart plus pembrolizumab in PROC may be explored in a randomized setting

1.Partnered with OncoC4;
PROC = platinum-resistant ovarian cancer

ESMO 2024 | Joyce N. Barlin, et. al., Phase 2 trial of BNT316/ONC-392 in platinum-resistant ovarian cancer (NCT05446298), Presentation LBA32

1

5

BNT113

HPV16+ Head and Neck Squamous Cell Carcinoma

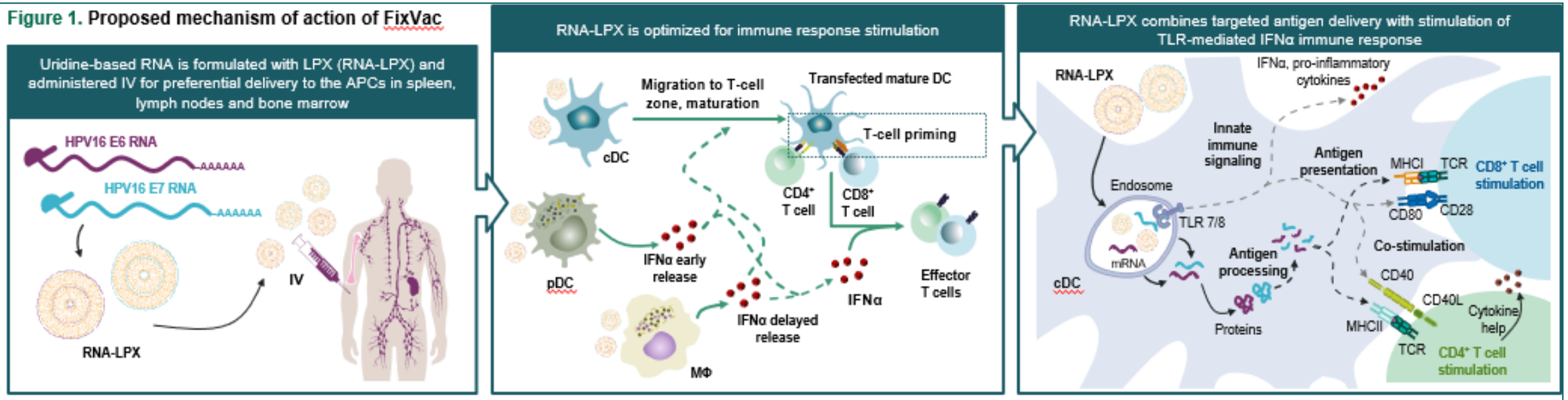
Exploratory analysis of antitumor activity and translational results from the safety run-in of AHEAD-MERIT, a Phase 2 trial of first-line pembrolizumab plus the fixed-antigen cancer vaccine BNT113 in advanced HPV16+ HNSCC

Nabil F. Saba, Department of Hematology and Medical Oncology, Emory University School of Medicine, Atlanta, GA, USA) et al.,
Presentation Number: 877P

BIONTECH

BNT113 FixVac Proposed Mechanism of Action

Figure 1. Proposed mechanism of action of FixVac



Background information:

- BNT113 is an investigational uridine-based mRNA-lipoplex (LPX) cancer immunotherapy encoding the human papillomavirus (HPV)16 oncoproteins E6 and E7[1,2]
- Intravenously administered RNA-LPX is preferentially delivered to dendritic cells (DCs), leading to DC maturation, activation of type I interferon (IFN)-driven immunity, and induction of profound antigen-specific T-cell responses (Figure 1)[3]
- The preliminary analysis of the safety run-in of AHEAD-MERIT suggested that BNT113 in combination with pembrolizumab was well tolerated; the safety profile was consistent with that expected for this combination[4]

1.PinattiLM, et al. J Dent Res. 2018; 97(6): 691–700; 2.Tran NH, et al. J Med Virol. 2024;96:e29746; 3. Kranz L, et al. Nature 2016;534:396–401; 4.Klinghammer K, et al. IOTECH 2022;16(suppl_1):19; doi: 10.1016/j.iotech.2022.100267.
APC = antigen-presenting cell; cDC = classical dendritic cell; DC = dendritic cell; HPV = human papillomavirus; IFN = interferon; IV = intravenous; LPX = lipoplex; NF-κB = nuclear factor kappa B; MΦ = macrophage; MHC =major histocompatibility complex; pD =, plasmacytoid dendritic cell; TCR = T-cell receptor; TLR = toll-like receptor.

ESMO 2024 | Nabil F. Saba, et. al., Exploratory analysis of antitumor activity of BNT113 in HNSCC (NCT04534205), Poster 877P

BIONTECH

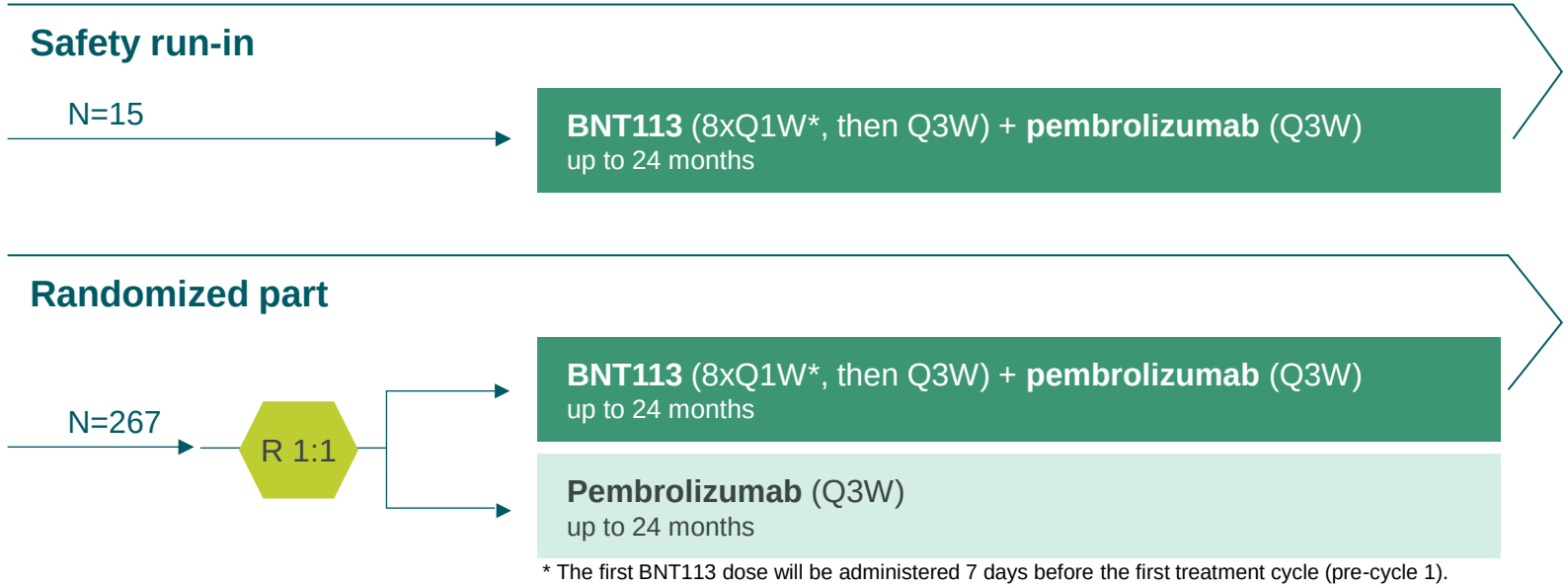
BNT113 in Combination with Pembrolizumab as 1L Treatment in Patients with R/R HPV16+ HNSCC Expressing PD-L1 (AHEAD-MERIT)

Phase 2 open-label, controlled study to confirm safety and efficacy of BNT113 in combination with pembrolizumab as 1L treatment in patients with metastatic HNSCC (NCT04534205)

Inclusion criteria

- Advanced, unresectable, recurrent or metastatic HNSCC
- Primary tumor locations oropharynx, oral cavity, hypopharynx, and larynx#
- Positive for HPV16 DNA
- Measurable disease per RECIST v1.1
- PD-L1 CPS ≥1
- ECOG PS 0 or 1

Patients with primary tumor site of nasopharynx were excluded



* The first BNT113 dose will be administered 7 days before the first treatment cycle (pre-cycle 1).

Endpoints

	Safety run-in	Randomized part
Primary:	TEAEs; *up to 27 months*	OS, ORR; *up to 48 months*
Secondary:	ORR, DoR, DCR	INV-ORR, PFS, DCR, DOR, safety
Exploratory:	PFS, OS, biomarkers	

1L = first line; CPS = combined positive score; DCR = disease control rate; DOR = duration of response; ECOG = Eastern Cooperative Oncology Group; INV = investigator assessed; iv = intravenously; HNSCC = head and neck squamous cell carcinoma; HPV16 = human papilloma virus 16; ORR = objective response rate; OS = overall survival; PD-L1 = programmed cell death protein ligand 1; PFS = progression free survival; Q3W = every three weeks; RECIST = Response Evaluation Criteria in Solid Tumors; R/M = recurrent/metastatic; R/R = relapsed/refractory; TEAE = treatment emergent adverse event.

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BIONTECH

BNT113 AHEAD-MERIT Trial Baseline Patient and Disease Characteristics – All Patients

Study status

As of 24 June 2024**, N=15 patients were enrolled** in the safety run-in part and received BNT113+pembrolizumab

Median exposure to BNT113 was 7.0 months (range, 1.6–24.4 months)

Characteristic	N=15
Age, median (range), years	66.0 (41–74)
Male, n (%)	15 (100)
ECOG PS=0, n (%)	10 (66.7)
ECOG PS=1, n (%)	5 (33.3)
Disease status, n (%)	
Metastatic disease	6 (40.0)
Unresectable recurrent	6 (40.0)
Metastatic and unresectable recurrent	2 (13.3)
Missing	1 (6.7)
PD-L1 CPS, n (%)	
CPS ≥20	7 (46.7)
CPS 1–<20	7 (46.7)
CPS <1[a]	1 (6.7)
Primary location, n (%)	
Hypopharynx	1 (6.7)
Larynx	0
Oral cavity	1 (6.7)
Oropharynx	13 (86.7)
Prior platinum (early setting)	11 (73.3)

Data cut-off: June 24, 2024.

a. Patient 104 was enrolled based on positive CPS. CPS = combined positive score; ECOG PS = Eastern Cooperative Oncology Group performance status; PD-L1 = programmed cell death ligand 1;

BNT113 in Combination with Pembrolizumab – Safety Profile

Safety observations

The safety analysis set included all 15 patients

The most frequently occurring TEAEs were pyrexia, chills, fatigue, nausea, influenza-like illness and hypothyroidism

There was one fatal TEAE of pulmonary sepsis (considered not related to study treatment)

Grade 3–4 TEAEs were reported in 7 patients (46.7%) and were considered related in 2 patients (13.3%):

- n=1 patient reported Grade 3 pyrexia and Grade 3 anemia; n=1 patient reported Grade 3 decreased appetite

Analysis of the safety run-in cohort of AHEAD-MERIT confirmed TEAEs were mostly Grade 1–2

	N=15[a]	
Patients reporting TEAE, n (%)	**All grades**	**Grade ≥3**
Any TEAE Number of events	15 (100) 309	8 (53.3) 18
Any related TEAE	15 (100)	2 (13.3)
Any TESAE		7 (46.7)
TESAE related to:		
BNT113 Pembrolizumab		2 (13.3) 3 (20.0)
Any TESAE leading to death		1 (6.7)[b]
Any TEAE leading to discontinuation of:		
BNT113 Pembrolizumab	0 1 (6.7)	

TEAEs reported in >1 patient[c]	**Grade 1–2**	**Grade 3–4**
Pyrexia	9 (60.0)	1 (6.7)
Chills	9 (60.0)	-
Fatigue	8 (53.3)	1 (6.7)
Nausea	5 (33.3)	-
Hypothyroidism	4 (26.7)	-
Influenza-like illness	4 (26.7)	-
Anemia	1 (6.7)	2 (13.3)
Decreased appetite	2 (13.3)	1 (6.7)
Constipation	3 (20.0)	-
Vomiting	3 (20.0)	-
Abdominal pain (upper)	1 (6.7)	1 (6.7)
Hypercalcemia	1 (6.7)	1 (6.7)
Back pain	2 (13.3)	-
Dermatitis acneiform	2 (13.3)	-
Dyspepsia	2 (13.3)	-
Headache	2 (13.3)	-
Hypertension	2 (13.3)	-
Tachycardia	2 (13.3)	-

Data cut-off: June 24, 2024.

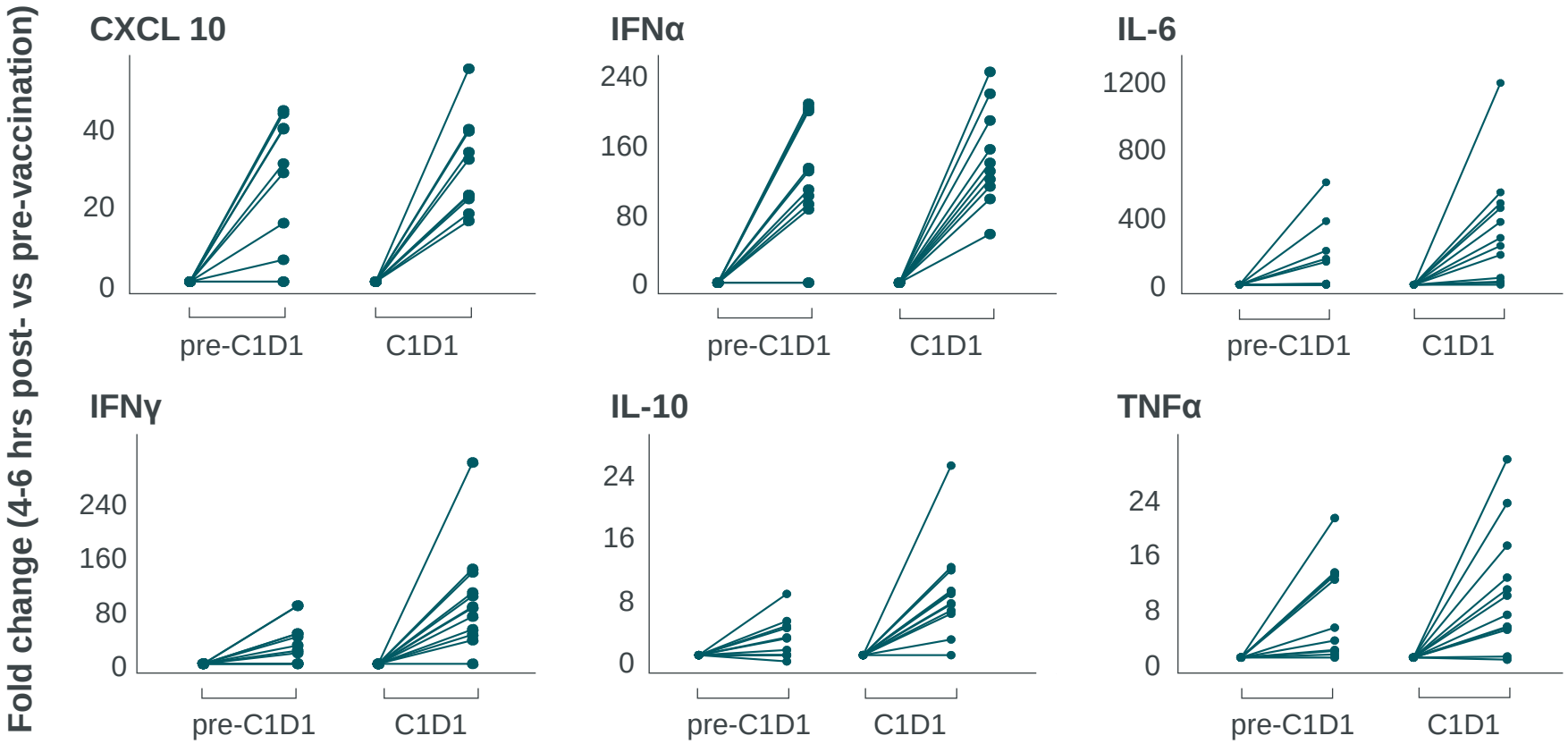
a. Analysis includes patient 104, who was enrolled based on local positive CPS; b. Pulmonary sepsis (n=1); c. The table shows TEAEs of any grade that were reported in >1 patient. The following TEAEs were reported in n=1 patient each as Grade 3–4: acute pancreatitis, cholangitis, cholangitis sclerosing, cholecystitis, circulatory collapse, decreased weight, duodenitis, gastritis, pleural effusion, pneumonia aspiration.
TEAE= treatment-emergent adverse event; TESAE = treatment-emergent serious adverse event.

ESMO 2024 | Nabil F. Saba, et. al., Exploratory analysis of antitumor activity of BNT113 in HNSCC (NCT04534205), Poster 877P

BIONTECH

BNT113 Triggered an Immune Response, Evidenced by Post-Vaccination Increase of Serum Levels of CXCL10, IFNα, IFNγ, IL-10, IL-6 and TNFα

Change in serum cytokine level – safety analysis set



Serum levels of cytokines (CXCL10, IFNα, IFNγ, IL-10, IL-6 and TNFα) increased 4–6 hours after BNT113 administration;

The range of increase was maintained when the vaccine was administered together with pembrolizumab

Individual patient data are shown as fold change in cytokine levels 4–6 hours post-versus pre-vaccination at pre-C1D1 (first BNT113 administration) and at C1D1 (BNT113 plus pembrolizumab administration).
Data were normalized to baseline; values below LLOQ were set to LLOQ/2.
C1D1 = cycle 1 day 1; CXCL = chemokine (C-X-C motif) ligand; IFN = interferon; IL = interleukin; LLOQ = lower limit of quantification; TNF = tumor necrosis factor..

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BIONTECH

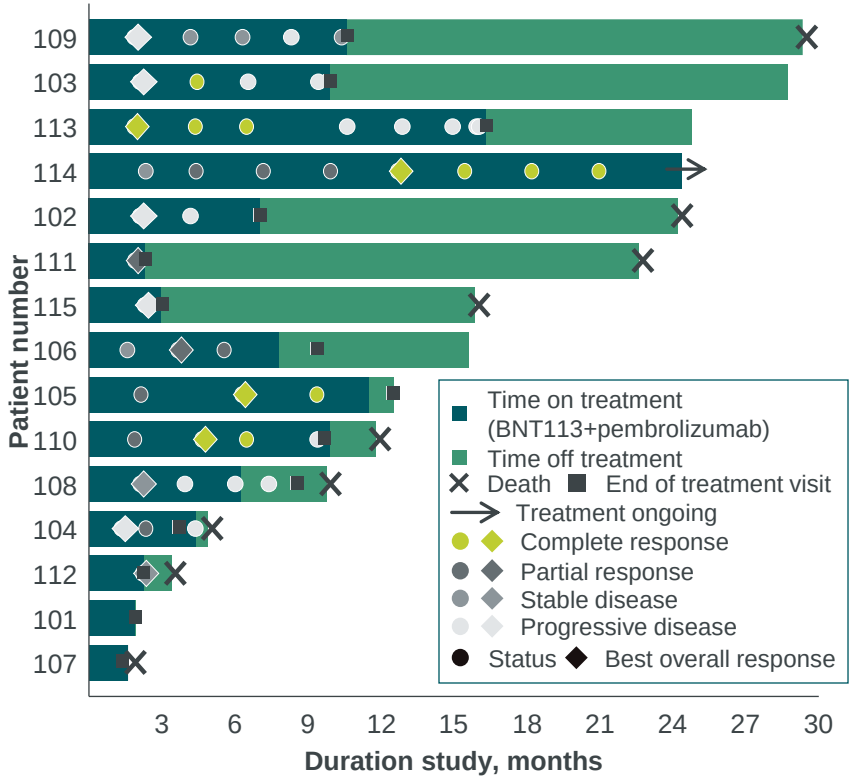
BNT113 Showed Encouraging Efficacy with Unconfirmed ORR (BICR) of 40%

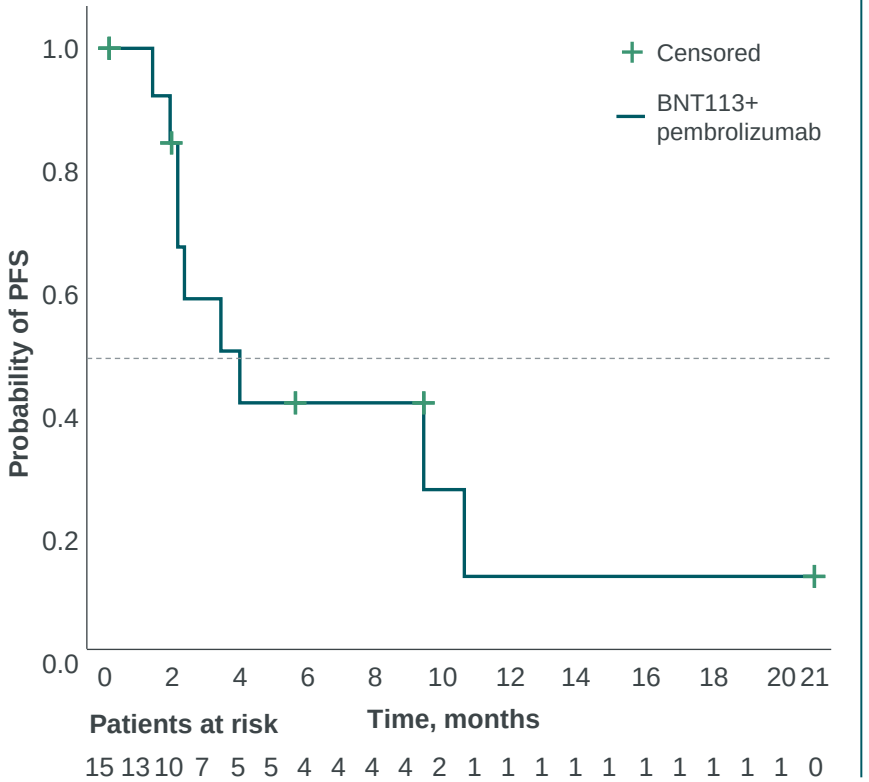
The efficacy analysis set was defined as all patients who received at least one dose of BNT113 (N=15)

Patient 104, who was enrolled based on local positive CPS result, was included in this analysis.

Antitumor activity	N=15
Unconfirmed ORR (BICR), %	40.0
CR, n	4
PR, n	2
Unconfirmed DCR (BICR), %	53.3
Unconfirmed ORR (investigator), %	33.3
Unconfirmed DCR (investigator), %	60.0
PFS by BICR	
Median (95% CI), months	3.9 (2.1–10.6)
6-month rate, %	42.3
12-month rate, %	14.1
18-month rate, %	14.1
PFS by investigator	
Median (95% CI), months	6.0 (2.3–10.4)
OS, median (95% CI), months	22.6 (9.8–NE)

Tumor overall response, treatment and survival status by BICR





Data cut-off: 24 June 2024

BICR = blinded independent central review; CI = confidence interval; CR = complete response; DCR = disease control rate; NE = not estimable; ORR = objective response rate; OS = overall survival; PFS = progression-free survival; PR = partial response.

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BNT113-Induced T-cell Response and Clonotype Expansion Post-Vaccination in Biomarker Cohort (n=3)

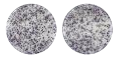
Summary of vaccine response measured ex vivo by IFNγELISpot and response per RECIST v1.1

	Best vaccine response per patient, cell type and target, measured by IFNγ ELISpot *ex vivo*						BOR per RECIST v1.1	
	PepMix E6			PepMix E7				
Patient	CD4+	CD8+	Bulk PBMC	CD4+	CD8+	Bulk PBMC	BICR	Inv.
109			■			■	PD	SD
111	■			■	■		PR	PD
115							PD	PD

■ Positive *de novo* response (*ex vivo* ELISpot) ▫ No response (*ex vivo* ELISpot)

The biomarker cohort included n=3 patients. A vaccine-induced T-cell response was observed in two patients (66.7%) against both E6 and E7 peptides of HPV16

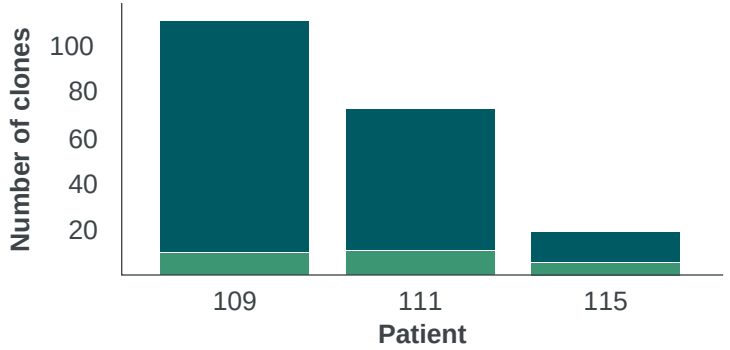
In patient 111, BNT113 induced both CD4+and CD8+T-cell responses

Target	Screening	C3D8
PepMix E6		
PepMix E7		

Example ELISpot images (Patient 109, bulk PBMCs at screening and at C3D8)

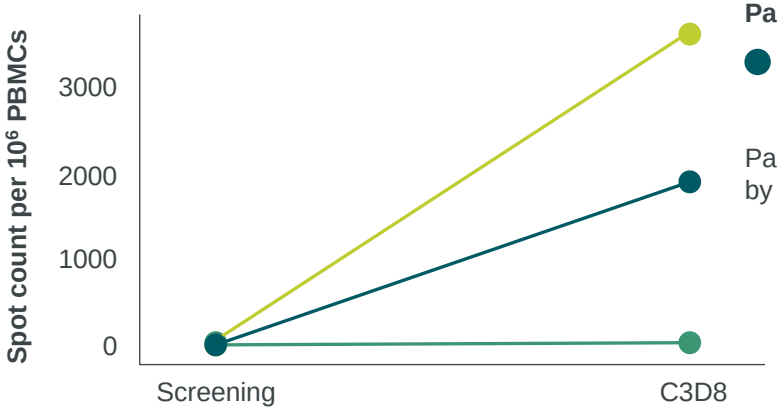
The normalized spot count of vaccine-induced T cells was highest in patient 111 (partial response [PR] per RECIST v1.1 by BICR), second highest in patient 109 (stable disease [SD] per RECIST v1.1 by investigator assessment), and lowest in patient 115, who had progressive disease

Number of significantly expanded TCR clones post-vaccination per patient



Expansion of *de novo* and pre-existing T-cell receptor (TCR) clonotypes was observed post-vaccination in all three patients.

Best immune response (*ex vivo* IFNγELISpot) per patient independent of cell type and target



Patient 109 had prolonged SD by investigator assessment.

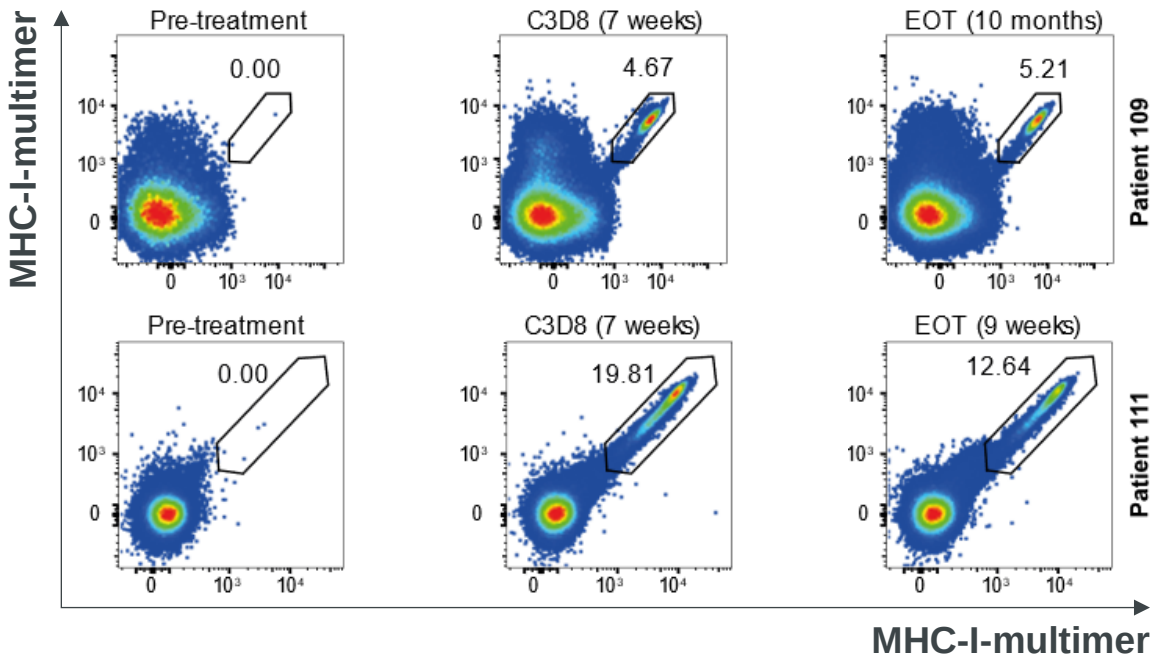
BICR = blinded independent central review; BOR = best overall response; C3D8 = cycle 3 day 8; Inv. = investigator assessment; IFN = interferon; PBMC = peripheral blood mononuclear cell; PD = progressive disease; PR = partial response; RECIST = Response Evaluation Criteria in Solid Tumors; SD = stable disease.

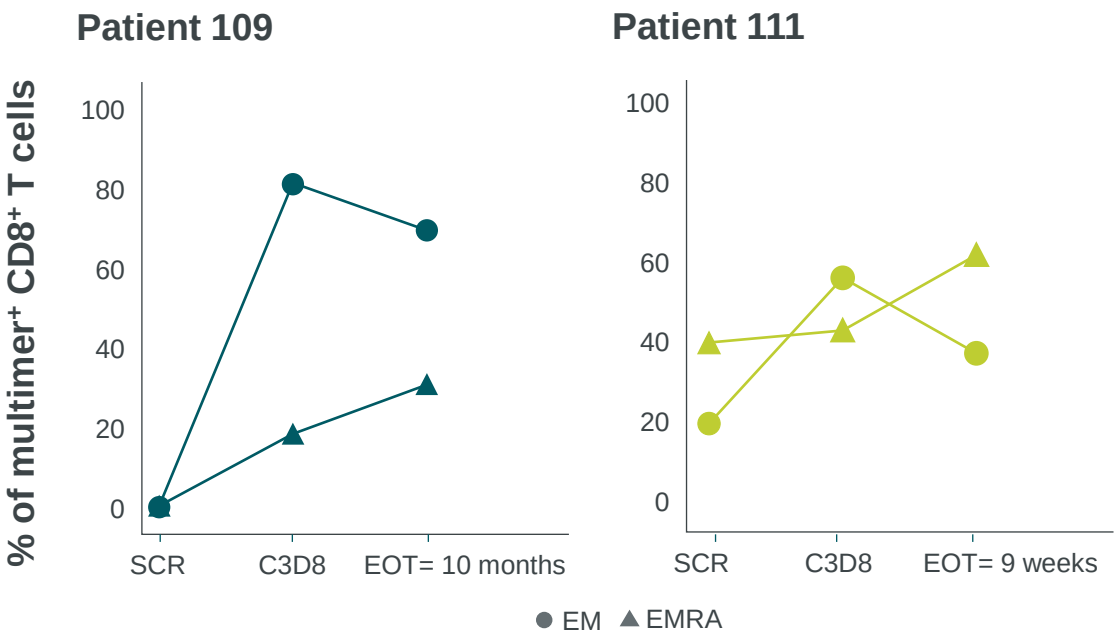
ESMO 2024 | Nabil F. Saba, et. al., Exploratory analysis of antitumor activity of BNT113 in HNSCC (NCT04534205), Poster 877P

BIONTECH

Large Portion of BNT113 Induced Antigen-Specific Peripheral T Cells had an Effector Memory Phenotype

Detection and phenotyping of vaccine antigen-specific peripheral T cells (n=2)





MHC-I-multimer staining of PBMCs revealed that, in two patients, **vaccine (E7) antigen-specific CD8+T cells** that appeared de novo by C3D8 **were detectable until the end of treatment** (10 months for patient 109 and 9 weeks for patient 111)

A large proportion of **vaccine antigen-specific multimer+CD8+T cells displayed an effector memory (EM) phenotype** with increasing CD45RA and CD57 positivity over time.

C3D8 = cycle 3 day 8; EMRA = effector memory T cells that re-express CD45RA; EOT = end of treatment; MHC = major histocompatibility complex; PBMC = peripheral blood mononuclear cell; SCR = screening;

ESMO 2024 | Nabil F. Saba, et. al., Exploratory analysis of antitumor activity of BNT113 in HNSCC (NCT04534205), Poster 877P

BNT113 (HPV16+ HNSCC) – ESMO 2024 Data: Key Takeaway Messages

Safety Profile:

Analysis of the safety run-in cohort confirmed combination of BNT113 and pembrolizumab was well tolerated:
TEAEs were mostly Grade 1–2

Efficacy:

Data from the biomarker cohort (n=3) showed that BNT113 induced *de novo* T-cell responses against HPV16 E6 and E7 antigens

- All three patients had an expansion of pre-existing or *de novo* TCR clonotypes post-vaccination; expansion was more pronounced in two patients who had T-cell response on *ex vivo* ELISpot
- In two patients with T-cell responses on *ex vivo* ELISpot, vaccine antigen-specific CD8+T cells were detectable in peripheral blood until the end of treatment
- A large proportion of vaccine antigen-specific peripheral T cells had an effector memory phenotype

ORR was 40.0% (BICR) and 33.3% (investigator), and median PFS was 3.9 months (BICR) and 6.0 months (investigator)

In the exploratory cohort, BNT113 triggered an immune response, as evidenced by a post-vaccination increase of serum levels of CXCL10, IFNα, IFNγ, IL-10, IL-6 and TNFα

Outlook:

The randomized part of the study is ongoing; patient recruitment is open in Argentina, Australia, Austria, Belgium, Brazil, Canada, Chile, Czech Republic, France, Germany, Hungary, Italy, Mexico, Poland, Portugal, Republic of Korea, Spain, Sweden, Taiwan, Turkey, the United Kingdom and the United States

BICR = blinded independent central review; CD = cluster of differentiation; CXCL = chemokine; HNSCC = head and neck squamous cell carcinoma; HPV16 = human papilloma virus 16; IFN = interferon; IL = interleukin; ORR = objective response rate; PFS = progression-free survival; TCR = T-cell response; TNF = tumor necrosis factor.

ESMO 2024 | Nabil F. Saba, et. al., Exploratory analysis of antitumor activity of BNT113 in HNSCC (NCT04534205), Poster 877P

1

6 BNT113 – HARE-40 (IIT)

HPV16+ Carcinomas

HARE-40: A phase I/II trial of therapeutic HPV vaccine (BNT113) in patients with HPV16 driven carcinoma

Christian H. Ottensmeier, MD, PhD, FRCP (Clatterbridge Cancer Centre NHS Foundation Trust, Liverpool, University of Liverpool, University of Southampton, UK) et al.; Presentation Number: 27LO

BIONTECH

BNT113 (FixVac) as HPV Anti-CD40 RNA Vaccine Monotherapy in Patients with HPV16+ Head and Neck Cancer and other HPV16+ Cancers (HARE-40) (IIT)

An Investigator-Initiated Phase 1/2 vaccine dose escalation study to evaluate safety, tolerability and recommended dose of BNT113 as monotherapy in patients with HPV16+ cancers (NCT03418480)

Arm 1A (n=17):

- HPV16+ HNSCC adjuvant

Cohort 1 → **BNT113, iv, Q1W x 4 then Q2W x 4**
Intra-patient dose escalation **from 7.2 µg to 29 µg**

Cohort 2 → **BNT113, iv, Q1W x 4 then Q2W x 4**
Intra-patient dose escalation **from 7.2 µg to 72.8 µg**

Arm 1B (n=13)*:

- HPV16+ advanced cancers, no SOC options
  - anal cancer (n=5)
  - HNSCC (n=3)
  - cervical (n=2)
  - other cancers (n=3)

*1 patient received DTH assessment but did not receive drug

→ **BNT113, iv, Q1W x 4 then Q2W x 4**
Intra-patient dose escalation **from 7.2 µg to 72.8 µg**

If clinically indicated, treatment **beyond dose 8** and **up to 1 year** allowed.

CD = cluster of differentiation; DTH = delayed type hypersensitivity; HNSCC = head and neck squamous cell carcinoma; HPV16+ = human papilloma virus 16-positive; IIT-investigator initiated trial; QxW = every x week; SOC = standard of care.

ESMO 2024 | Chr. H. Ottensmeier, et. al., HARE-40: Phase I/II trial of BNT113 in HPV16+ carcinoma (NCT03418480), Presentation 999MMO

BNT113 was Overall Well Tolerated with Manageable Safety Profile

Common AEs (≥20%), n (%)	N=30	Event grade ≥3
Nausea	13 (43%)	0
Fatigue	13 (43%)	1
Headache	12 (40%)	0
Chills	7 (23%)	0
Constipation	6 (20%)	1
Back pain	6 (20%)	0
Cough	6 (20%)	0

- N=30 patients were included in the safety analysis
- 19/30 (63%) patients received 8 doses of BNT113
- 2 patients in Arm 1A met individual MTD[a]
- No SAE with fatal outcome

[a] These patients did not experience a DLT but met their individual MTD as defined by the Safety Review Committee.

Reason for treatment discontinuation, n (%)	N=30
Subject withdrawal	5 (17%)
Disease progression	2 (7%)
Unacceptable toxicity	1 (3%)
Other/missing	3 (10%)

Related AEs, n (%)	Grade	N=30
Within 1 week	≥1	26 (87%)
Within 90 days	≥3	7 (23%)
(Pre)-Syncope		4 (one patient)
Fatigue		1
IRR[b]		1
Hypotension		2

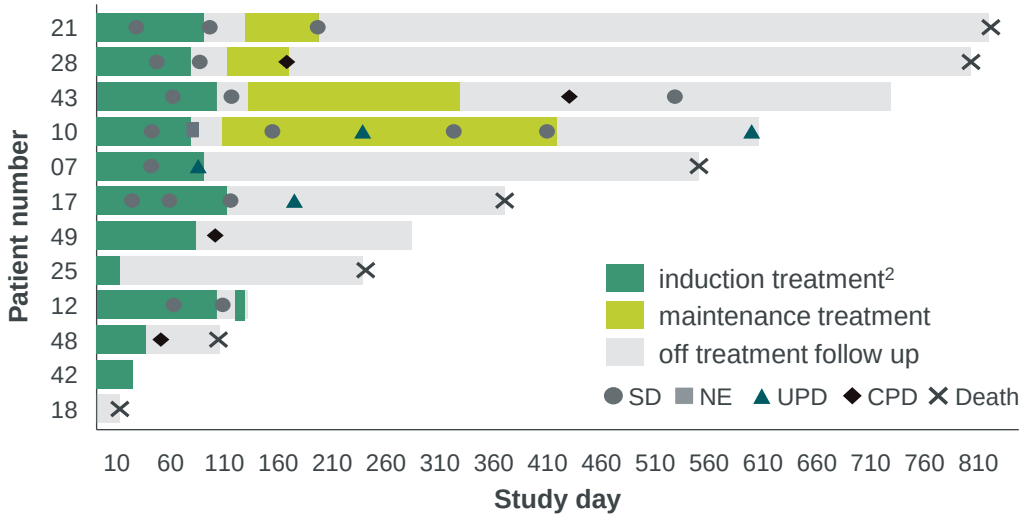
[b] Includes patients reporting preferred term IRR per CTCAE Version 4.03.

AE = adverse event; CTCAE = Common Terminology Criteria for Adverse Events; DLT = dose limiting toxicity; IRR = infusion-related reaction; MTD = maximum tolerated dose; SAE = serious adverse event.

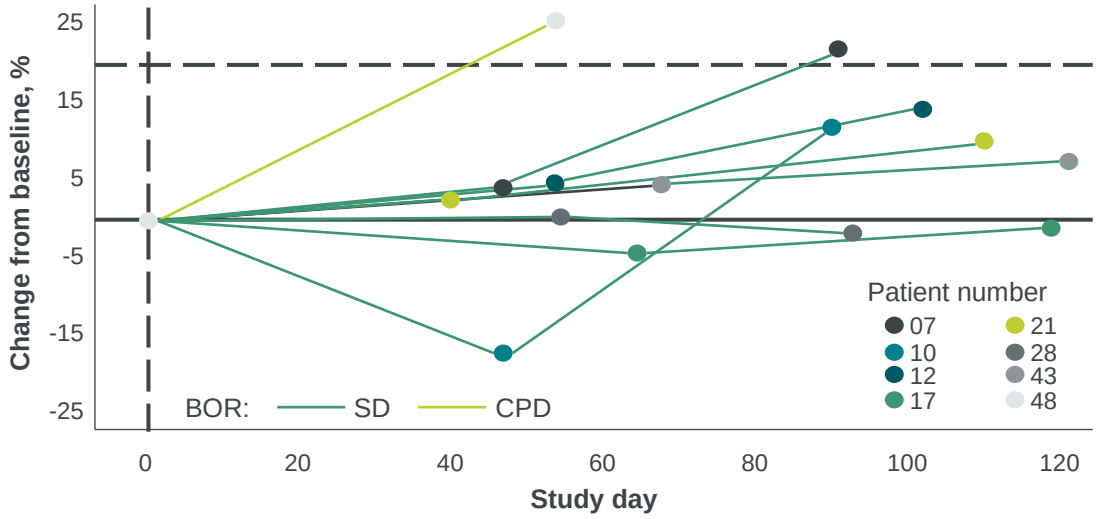
ESMO 2024 | Chr. H. Ottensmeier, et. al., HARE-40: Phase I/II trial of BNT113 in HPV16+ carcinoma (NCT03418480), Presentation 999MMO

BNT113: Preliminary Efficacy Assessment

Time of treatment, disease response[1], and follow-up in arm 1B



Change of irRECIST target lesion from baseline until EoT – arm 1B



- Median follow up in Arm 1B: 26.5 months
- DCR at EoT: 71% (95% CI: 29-96%, 7 evaluable patients)
- 5 patients received maintenance treatment in Arm 1B

Disease response[1] at EoT, n (%)	**N=9**
Stable disease	5 (71%)
Unconfirmed progression	1 (14%)
Confirmed progression	1 (14%)
Not evaluable	1
Missing eCRF	1

1 Responses evaluated per irRECIST. 2. Time until end of induction treatment visit is depicted. BOR = best overall response; CI = confidence interval; CPD = confirmed progression; DCR = disease control rate; eCRF = electronic case report form; EoT = end of treatment; irRECIST = Immune-related Response Evaluation Criteria In Solid Tumors; NE = not evaluable; SD = stable disease; UPD = unconfirmed progression.

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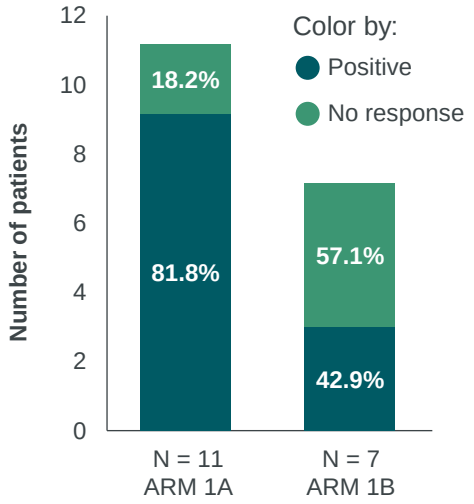
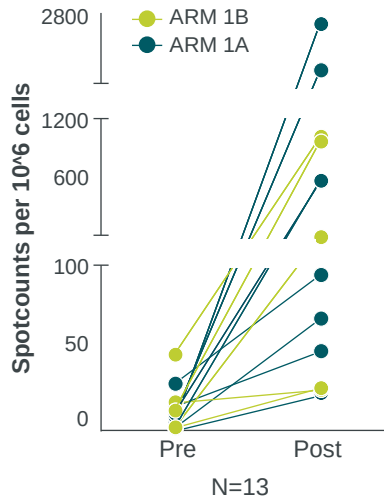
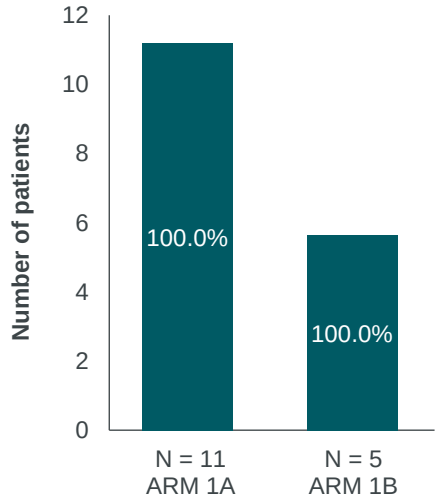
BNT113 Showed Immune Responses in Adjuvant and Advanced Disease

ex vivo IFNγ ELISpot responses to E6 and/or E7 peptide pools

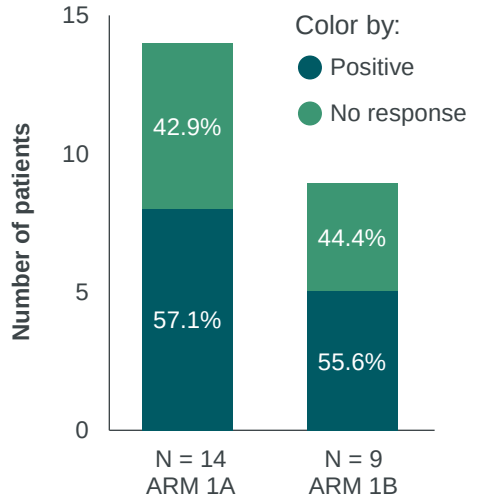




ivS IFNγ ELISpot responses to E6/E7 peptide pools



Anti-E7 IgG antibody responses (ELISA)



- 66.7% (12/18 evaluable patients): vaccine-induced E6/E7 responses by ex-vivo ELISpot. 9/11 in Arm 1A; 3/7 in Arm 1B
- 100% (16/16 evaluable patients): IFNγ E6/E7 response by post *ivS* ELISpot assay
- Anti E7 IgG antibody response in ~56% of patients in both arms

APC = antigen presenting cell; ELISA = enzyme-linked immunosorbent assay; IgG = immunoglobulin G; IFN = interferon; IL = interleukin; ivS = in vitro stimulation

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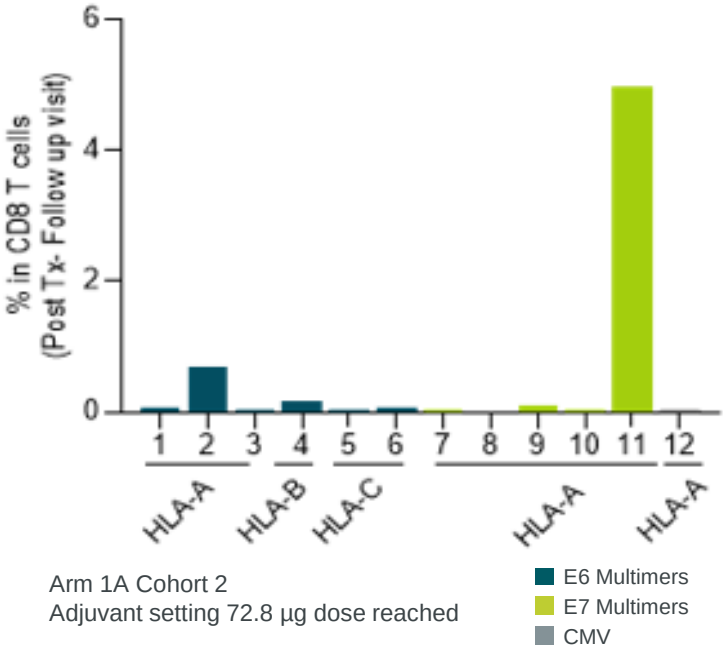
BIONTECH

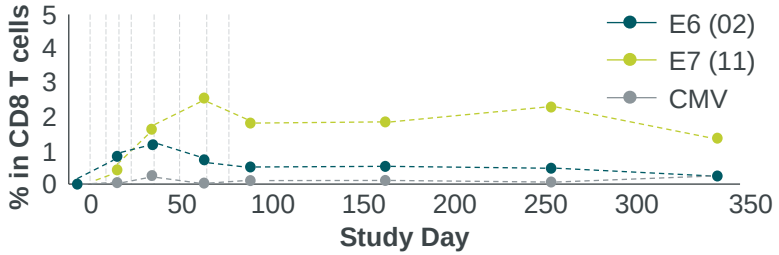
BNT113 Vaccine-Induced T cell Tracking and Phenotypic Characterization

Individual patient multimer screening

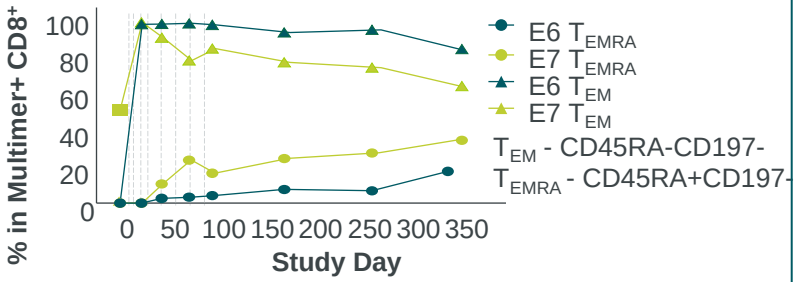


Arm 1A Cohort 2
Adjuvant setting 72.8 µg dose reached

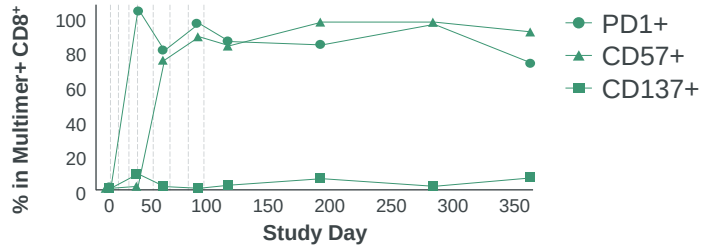
Kinetic assessment of multimer^{+}CD8^{+} T cells



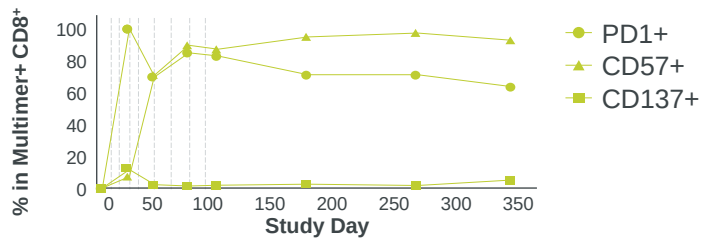
Phenotype of multimer^{+}CD8^{+} T cells



Phenotype of E6 multimer+CD8+ T cells



Phenotype of E7 multimer+CD8+ T cells



Vaccination marked on timeline as vertical grey dotted lines.
At study day 0, <6 multimer events+ were detected in the gate in all samples

- Vaccine-induced CD8^{+}multimer^{+}: up to 4.98% of CD8 T cells in PBMC
- CD8^{+}multimer^{+}: effector memory (CD197-CD45RA-) with PD-1 and CD57 expression

CMV = cytomegalovirus; EM = effector memory; EMRA = effector memory T cells that re-express CD45RA; HLA = human leukocyte antigen; PBMC = peripheral blood mononuclear cell; PD-1 = programmed death-1.

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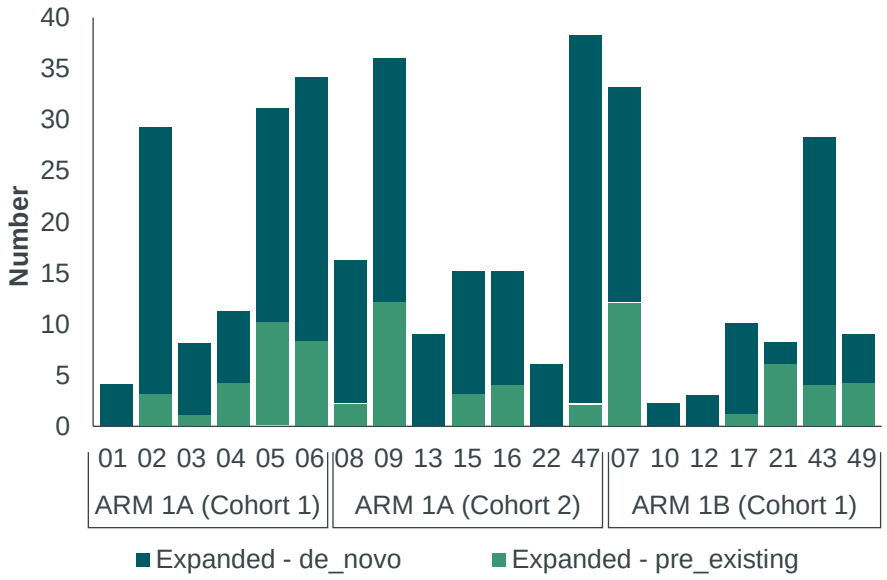
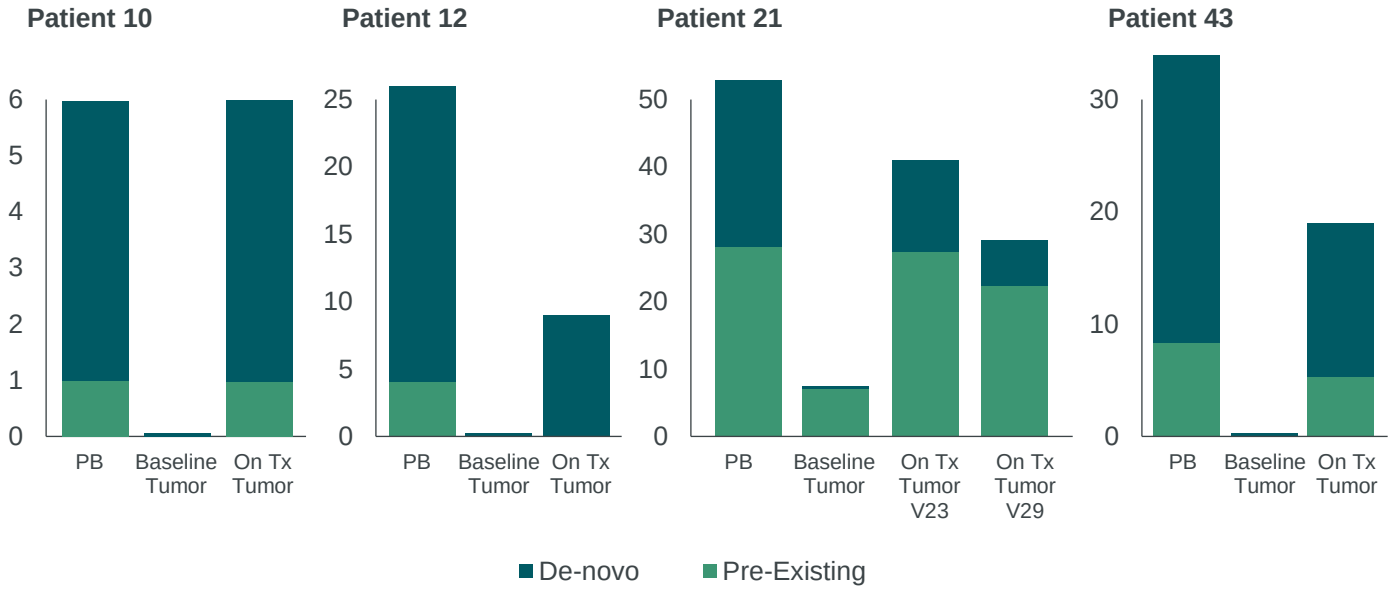
BNT113: Kinetic TCR Profiling in PBMC and Tumor

Profiling of TCR clones in periphery (significantly expanded clones)



Tracking of expanded clonotypes of periphery in tumor tissue collected at baseline and on-treatment



- Expansion of *de novo* and pre-existing TCR clonotypes was observed post vaccination in patients from all three cohorts
- T cell clonotypes expanded in peripheral blood could be tracked in on-treatment (Tx) tumor, but rarely in baseline tumor
- TCRs found in tumor have been validated to be specific-against HPV16 E6/E7[1]

1. Data not shown.
Tx = on-treatment.; PV = human papilloma virus; PB = peripheral blood; PBMC = peripheral blood mononuclear cell; TCR = T-cell receptor

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BNT113 (HPV16+ carcinomas) – ESMO 2024 Data: Key Takeaway Messages

Safety Profile:

BNT113 – investigational mRNA vaccine encoding HPV16 E6/E7 – was overall well tolerated and had a manageable safety profile

Efficacy:

- T cell induction against both E7 and E6
  - Pre-existing and *de novo* effector T-cell responses were detected *ex vivo* (more pronounced in the adjuvant setting vs advanced disease)
  - Vaccine-induced T cells of effector memory phenotype persisted in circulation beyond treatment period
  - In patients with advanced disease, *de novo* vaccine-induced T cells migrate to tumor post-vaccination
- The vaccine was immunogenic in both the adjuvant and end-stage clinical setting
- In Arm 1B, DCR was 71%

Outlook:

Further studies are needed to fully assess the clinical activity of BNT113

DCR = disease control rate; HPV16 = human papilloma virus 16.

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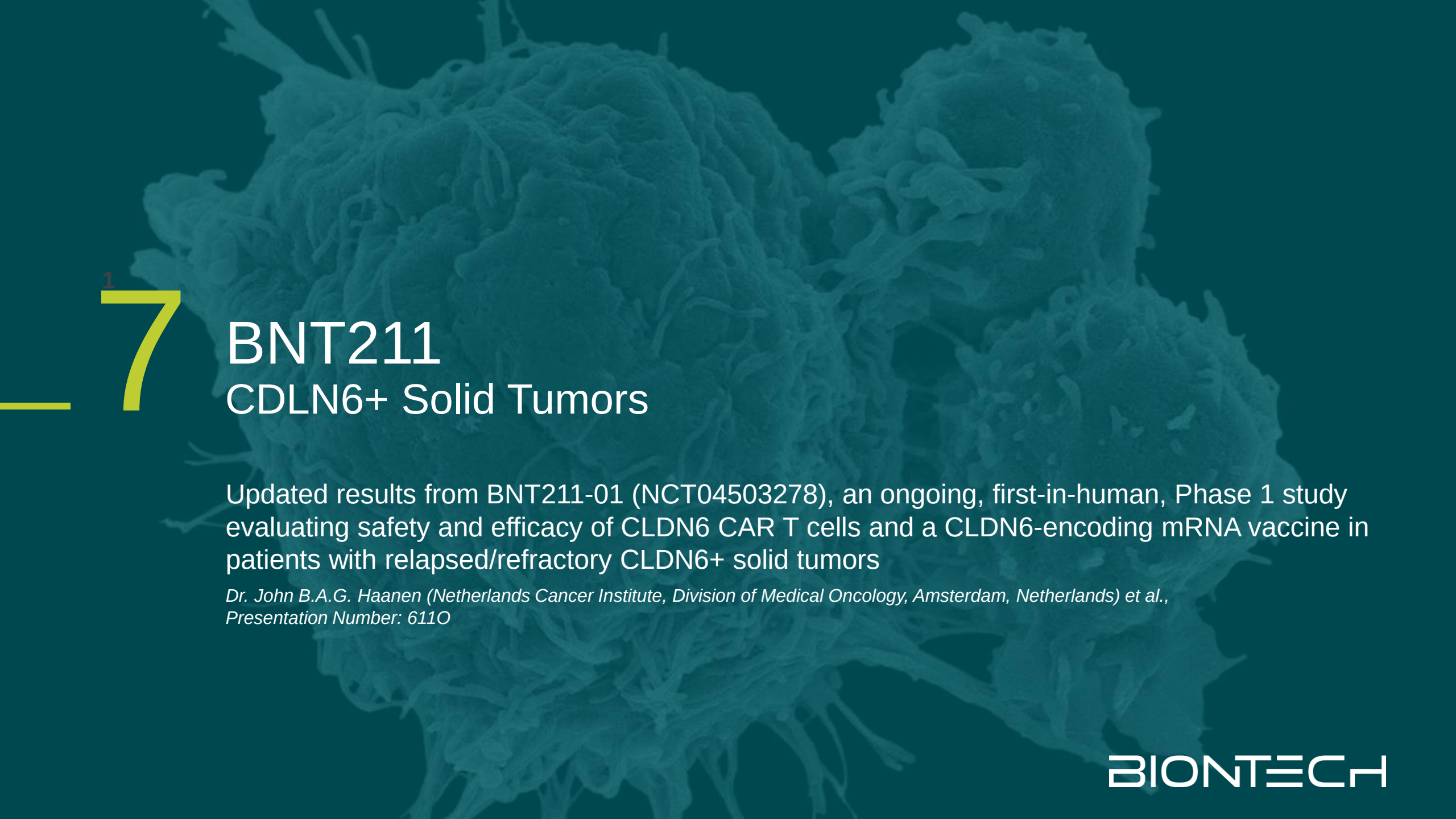


17

BNT211

CDLN6+ Solid Tumors

Updated results from BNT211-01 (NCT04503278), an ongoing, first-in-human, Phase 1 study evaluating safety and efficacy of CLDN6 CAR T cells and a CLDN6-encoding mRNA vaccine in patients with relapsed/refractory CLDN6+ solid tumors

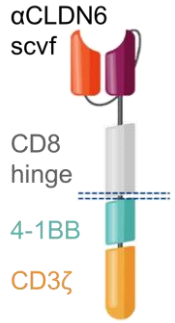
Dr. John B.A.G. Haanen (Netherlands Cancer Institute, Division of Medical Oncology, Amsterdam, Netherlands) et al.,
Presentation Number: 611O

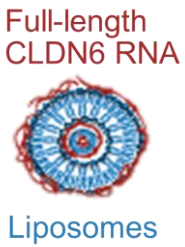
BIONTECH

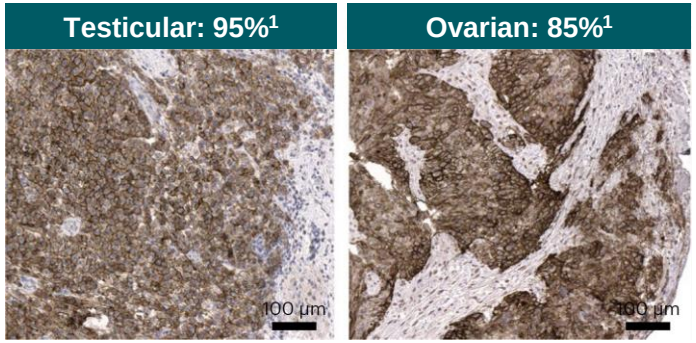
BNT211 – A Potentially First-in-Class Approach for CLDN6+ Solid Tumors

Second generation CAR targeting CLDN6, an oncofetal antigen

CLDN6 CAR T[1,2] ± CLDN6 CARVac[3,4]

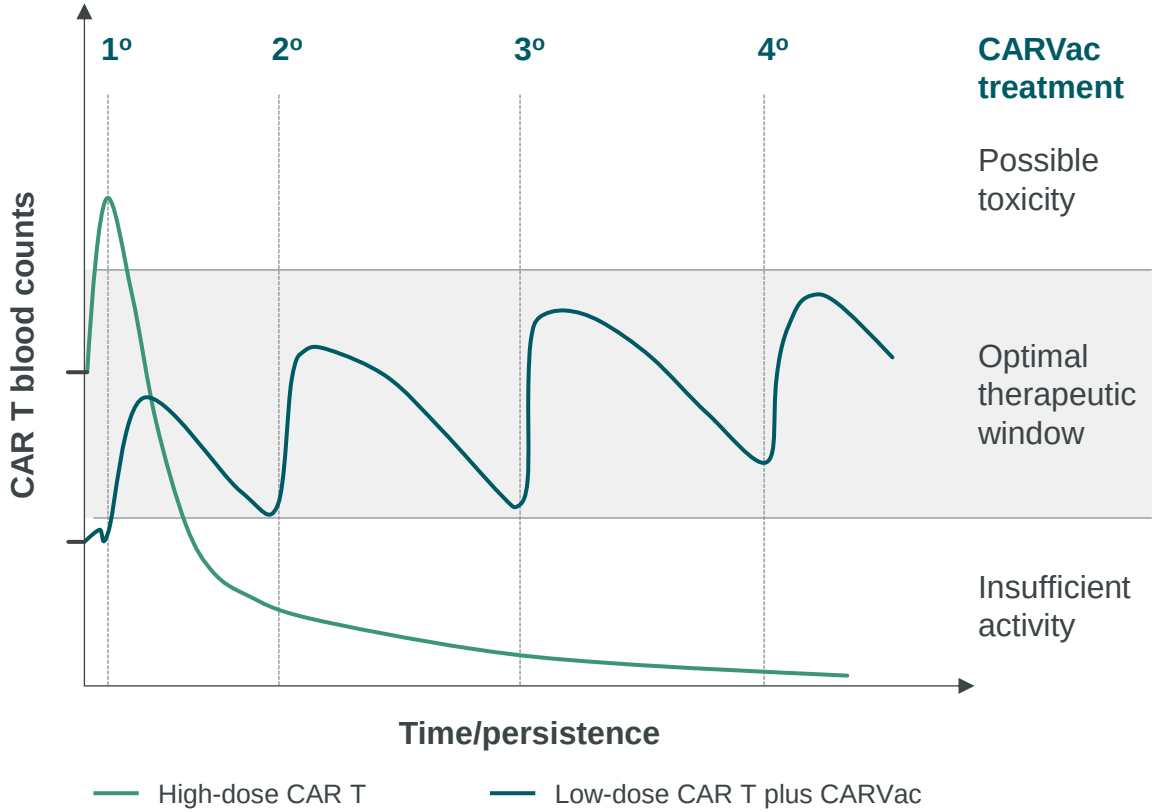






CLDN6 is an oncofetal antigen, expressed during fetal organogenesis and overexpressed in many solid tumors yet absent in healthy adult tissues[1]

Scientific rationale and concept of CARVac-driven expansion of CAR T cells[3]



1. Mackensen A, et al. Nature Med 2023;29:2844–2853; 2. Haanen JBAG, et al. Ann Oncol 2023;34 (suppl_2):S1281–S1282; 3. Reinhard K, et al. Science 2020;367:446–453; 4. Sahin U, et al. Nature 2020;585:107–112.
CAR = chimeric antigen receptor; CARVac = CAR T-cell amplifying RNA vaccine; CD = cluster of differentiation; CLDN6 = Claudin 6; scvf = single-chain variable fragment.

BNT211 as Monotherapy or in Combination with Ribonucleic Acid Lipoplexes (RNA-LPX) in Patients with CLDN6-Positive Advanced Solid Tumors

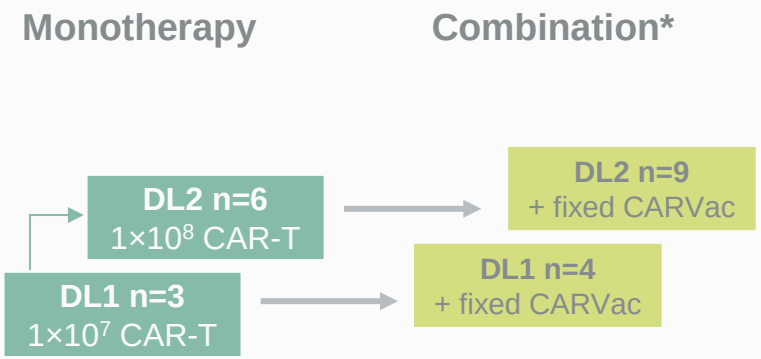
Phase 1, FIH, open-label, dose escalation study with expansion cohort to evaluate safety and efficacy of BNT211 with/without RNA-LPX in patients with CLDN6+ R/R solid tumors (NCT04503278)

Inclusion criteria

- ≥50% tumor cells with CLDN 6 IHC 2+/3+ CLDN6 positivity (immunohistochemistry)
- Measurable disease per RECIST v1.1 or elevated tumor marker
- ECOG PS 0–1

ESMO 2022

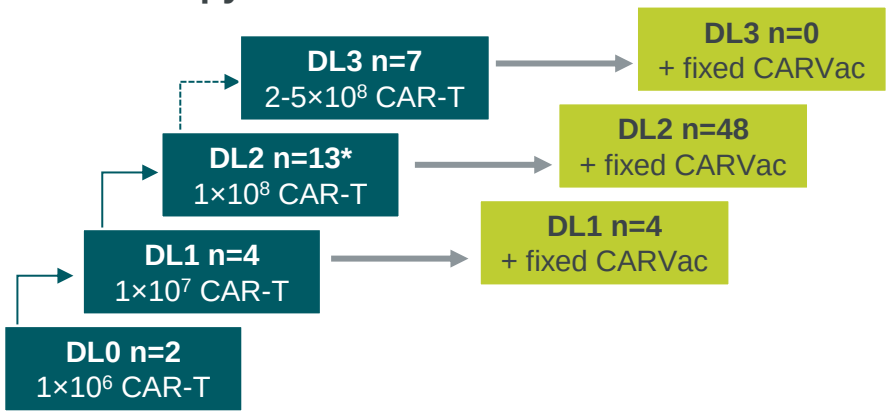
Part A: Manual product (n=22; completed)[1]



Published in:
Mackensen et al., Nature Medicine, 2023

ESMO 2023

Part B: Automated product (n=78; ongoing)[2]



*[a]Three patients were treated at an optional de-escalation dose (DL 1.5=5×10^7 cells) to further evaluate clinical safety and efficacy.

Key endpoints

Primary: Safety & tolerability, MTD, RP2D
Secondary: ORR, DCR, DOR

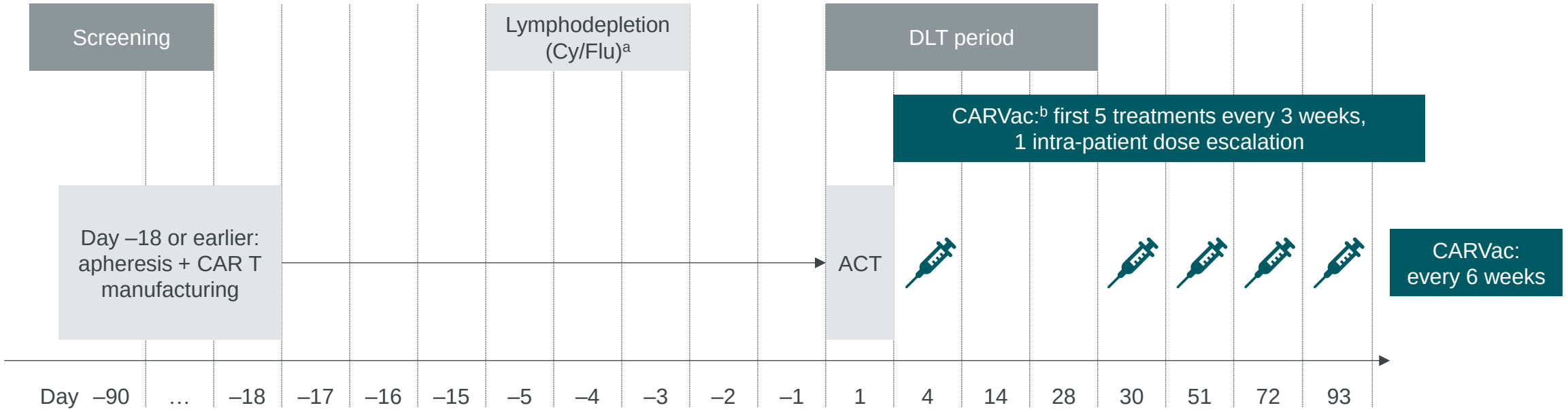
1. Mackensen A, et al. Nature Med 2023;29:2844–2853; 2. Haanen JBAG, et al. Ann Oncol 2023;34 (suppl_2):S1281–S1282.
CAR = chimeric antigen receptor; CLDN6 = Claudin 6; DCR = disease control rate; DLx = dose level x; DOR = duration of response; ECOG = Eastern Cooperative Oncology Group; FIH = first in human; IHC = immunohistochemistry; MTD = maximum tolerated dose; ORR = objective response rate; RECIST = Response Evaluation Criteria in Solid Tumors; RP2D: recommended Phase 2 dose; R/R = relapsed/refractory.

Dose Escalation Scheme for Automated Cell Product Candidate

Dose escalation was performed with cell products from a **manual** process (n=22; completed)[1] and an **automated** process[2] (n=78 in the current analysis; ongoing)

Dose escalation scheme for cell product candidate derived from automated process

Patients with R/R advanced CLDN6+ solid tumors



1. Mackensen A, et al. Nature Med 2023;29:2844–2853; 2. Haanen JBAG, et al. Ann Oncol 2023;34 (suppl_2):S1281–S1282.
aThree patients were treated at an optional de-escalation dose (DL 1.5=5×107 cells) to further evaluate clinical safety and efficacy. bThe starting dose of CARVac dose was 50 µg, with one intra-patient escalation to 100 µg.
ACT = adoptive cell transfer; CAR = chimeric antigen receptor; CARVac = CAR T-cell amplifying RNA vaccine; CLDN6 = claudin-6; Cy/Flu = cyclophosphamide /fludarabine; DLT = dose limiting toxicity; .

BNT211-01: Baseline Characteristics – Safety Set

Presented are data from N=78 patients who received automated process CAR T

Dose level (number of CAR T cells)	CAR T only					CAR T + CARVac				
	DL0 ($1x10^6$)	DL1 ($1x10^7$)	DL1.5 ($5x10^7$)	DL2 ($1x10^8$)	DL3 ($2–5x10^8$)	DL1 ($1x10^7$)	DL2 ($1x10^8$)	DL2 ($1x10^8$)	DL2 ($1x10^8$)	
LD (Flu/Cy)	**100%**	**100%**	**100%**	**100%**	**100%**	**100%**	**50%**	**75%**	**100%**	
Patients, n (%) / Characteristic	**(n=2)**	**(n=4)**	**(n=3)**	**(n=10)**	**(n=7)**	**(n=4)**	**(n=6)**	**(n=15)**	**(n=27)**	**N=78**
Median age (range), years	55.5 (50–61)	54.5 (36–62)	46.0 (34–54)	47.5 (30–69)	48.0 (29–63)	51.0 (42–65)	36.0 (26–60)	54.0 (29–68)	46.0 (19–69)	48.0 (19–69)
Female, n (%)	1 (50.0)	1 (25.0)	1 (33.3)	5 (50.0)	3 (42.9)	2 (50.0)	3 (50.0)	8 (53.3)	12 (44.4)	36 (46.2)
CLDN6 2+/3+ cells, % Median (range)	82.5 (80–85)	97.5 (80–100)	90.0 (80–95)	95.0 (50–100)	90.0 (55–100)	97.5 (50–100)	79.5 (50–100)	90.0 (50–100)	85.0 (50–100)	90.0 (50–100)
Cancer type										
Testicular/GCT[a]	**1 (50.0)**	**0**	**2 (66.7)**	**3 (30.0)**	**3 (42.9)**	**1 (25.0)**	**3 (50.0)**	**7 (46.7)**	**10 (37.0)**	**30 (38.4)**
Ovarian	**1 (50.0)**	**1 (25.0)**	**1 (33.3)**	**5 (50.0)**	**2 (28.6)**	**2 (50.0)**	**2 (33.3)**	**7 (46.7)**	**10 (37.0)**	**31 (39.7)**
Sarcoma[b]	0	1 (25.0)	0	0	0	0	1 (16.7)	0	4 (14.8)	6 (7.7)
Lung	0	0	0	2 (20.0)	0	1 (25.0)	0	0	1 (3.7)	4 (5.1)
Esophageal/GEJ	0	2 (50.0)	0	0	1 (14.3)	0	0	0	0	3 (3.8)
Other[c]	0	0	0	0	1 (14.3)	0	0	1 (6.7)	2 (7.4)	4 (5.1)
Median prior lines (range)	3 (2–4)	4 (3–7)	5 (3–6)	3.5 (2–5)	4 (3–5)	4.5 (2–9)	3.5 (2–9)	4 (1–8)	4 (2–11)	4 (1–11)

[a] Includes seminoma, non-seminoma, extragonadal GCTs. [b] Includes desmoplastic sarcoma and epitheloid sarcoma. [c] Includes breast cancer, pancreatic cancer, sinunasal carcinoma and uterine cancer (n=1 each).

Data cut-off: May 16, 2024.

CAR = chimeric antigen receptor; CARVac = CAR T-cell amplifying RNA vaccine; CLDN6 = claudin-6; DL = dose level; GCT = germ cell tumor; GEJ = gastro-esophageal junction; LD = lymphodepletion.

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BNT211 Showed Consistent Safety Profile1-3 and No Increased Toxicity with Repeated CARVac Administration

With respect to safety results, we observed a CAR-T dose dependency

Dose level (number of CAR T cells)	CAR T only					CAR T + CARVac				
	DL0 ($1x10^6$)	DL1 ($1x10^7$)	DL1.5 ($5x10^7$)	DL2 ($1x10^8$)	DL3 ($2–5x10^8$)	DL1 ($1x10^7$)	DL2 ($1x10^8$)	DL2 ($1x10^8$)	DL2 ($1x10^8$)	
LD (Flu/Cy)	**100%**	**100%**	**100%**	**100%**	**100%**	**100%**	**50%**	**75%**	**100%**	
Patients, n (%)	**(n=2)**	**(n=4)**	**(n=3)**	**(n=10)**	**(n=7)**	**(n=4)**	**(n=6)**	**(n=15)**	**(n=27)**	**N=78**
Any TEAE	2 (100)	4 (100)	3 (100)	10 (100)	7 (100)	4 (100)	6 (100)	15 (100)	27 (100)	78 (100)
Grade ≥3	2 (100)	4 (100)	3 (100)	10 (100)	7 (100)	3 (75.0)	5 (83.3)	13 (86.7)	24 (88.9)	71 (91.0)
Any SAE	1 (50.0)	2 (50.0)	3 (100)	4 (40.0)	4 (57.1)	2 (50.0)	4 (66.7)	9 (60.0)	16 (59.3)	45 (57.7)
Any TRAE[a]	2 (100)	2 (50.0)	3 (100)	10 (100)	7 (100)	4 (100)	5 (83.3)	14 (93.3)	25 (92.6)	72 (92.3)
Grade ≥3[a]	1 (50.0)	1 (25.0)	3 (100)	10 (100)	6 (85.7)	1 (25.0)	2 (33.3)	9 (60.0)	19 (70.4)	52 (66.7)
Any related SAE	1 (50.0)	-	3 (100)	3 (30.0)	3 (42.9)	-	1 (16.7)	5 (33.3)	10 (37.0)	26 (33.3)
Fatal TEAE	-	-	1 (33.3)	2 (20.0)	1 (14.3)	-	-	1 (6.7)	2 (7.4)	7 (9.0)
Related[a]	-	-	-	2 (20.0)	-	-	-	-	1 (3.7)	3 (3.8)
TEAE leading to treatment discontinuation	-	-	-	-	-	-	-	1 (6.7)	1 (3.7)	2 (2.6)
DLT	-	-	1 (33.3)	1 (10.0)	1 (14.3)	-	-	1 (6.7)	3 (11.1)	7 (9.0)

[a] Includes AEs related to CLDN6 CAR T and/or CARVac; does not include events related to LD chemotherapy. Fatal TEAEs related to CAR T ± CARVac included sepsis, fungal pneumonia and HLH (n=1 each). DLTs included HLH/IEC-HS, liver toxicity, cytopenia and CRS.

Data cut-off: May 16, 2024.

CAR = chimeric antigen receptor; CARVac = CAR T-cell amplifying RNA vaccine; CLDN6 = claudin-6; Cy = cyclophosphamide; DL = dose level; DLT = dose-limiting toxicity; Flu = fludarabine; HLH = hemophagocytic lymphohistiocytosis; IEC-HS = immune effector cell-associated HLH-like syndrome; LD = lymphodepletion; SAE = serious adverse event; TEAE = treatment-emergent adverse event; TRAE = treatment-related adverse event.

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BNT211-01: AEs Associated with CAR T Treatment Class – Safety Set

CRS was mostly grade 1 or 2 (only 2 patients saw Gr 3 or above) and all cases of ICANS were grade 1

Dose level (number of CAR T cells)	CAR T only					CAR T + CARVac				
	DL0 ($1x10^6$)	DL1 ($1x10^7$)	DL1.5 ($5x10^7$)	DL2 ($1x10^8$)	DL3 ($2–5x10^8$)	DL1 ($1x10^7$)	DL2 ($1x10^8$)	DL2 ($1x10^8$)	DL2 ($1x10^8$)	
LD (Flu/Cy)	**100%**	**100%**	**100%**	**100%**	**100%**	**100%**	**50%**	**75%**	**100%**	
Patients, n (%)	**(n=2)**	**(n=4)**	**(n=3)**	**(n=10)**	**(n=7)**	**(n=4)**	**(n=6)**	**(n=15)**	**(n=27)**	**N=78**
CRS[a] Grade 1–2	1 (50.0)	-	2 (66.7)	6 (60.0)	5 (71.4)	2 (50.0)	4 (66.7)	12 (80.0)	18 (66.7)	50 (64.1)
Grade ≥3	-	-	-	-	1 (14.3)	-	-	-	1 (3.7)	2 (2.6)
ICANS Grade 1–2	-	-	-	1 (10.0)	-	-	1 (16.7)	-	1 (3.7)	3 (3.8)
Grade ≥3	-	-	-	-	-	-	-	-	-	-
Any HLH/IEC-HS	-	-	-	2 (20.0)	2 (28.6)	-	-	3 (20.0)	6 (22.2)	13 (16.7)
Grade ≥3	-	-	-	2 (20.0)	2 (28.6)	-	-	1 (6.7)	3 (11.1)	8 (10.3)
Prolonged cytopenias[b]	1 (50.0)	3 (75.0)	3 (100)	6 (60.0)	4 (57.1)	2 (50.0)	1 (16.7)	7 (46.7)	15 (55.6)	42 (53.8)
Anemia	1 (50.0)	1 (25.0)	-	2 (20.0)	1 (14.3)	-	1 (16.7)	2 (13.3)	9 (33.3)	17 (21.8)
Leukopenia	-	-	1 (33.3)	1 (10.0)	1 (14.3)	-	-	-	6 (22.2)	9 (11.5)
Lymphopenia	-	1 (25.0)	-	4 (40.0)	1 (14.3)	2 (50.0)	-	2 (13.3)	5 (18.5)	15 (19.2)
Neutropenia	-	-	-	-	2 (28.6)	-	-	3 (20.0)	-	5 (6.4)
Thrombocytopenia	1 (50.0)	1 (25.0)	1 (33.3)	2 (20.0)	2 (28.6)	1 (25.0)	-	3 (20.0)	5 (18.5)	16 (20.5)
Pancytopenia	-	-	1 (33.3)	1 (10.0)	-	-	-	-	2 (7.4)	4 (5.1)

[a] Per American Society for Transplantation and Cellular Therapy (ASTCT) grading guidelines.
[b] Grade 3 or 4 cytopenia that has not recovered to Grade ≤ 2 by day 30±2 days after ACT.

Data cut-off: May 16, 2024.

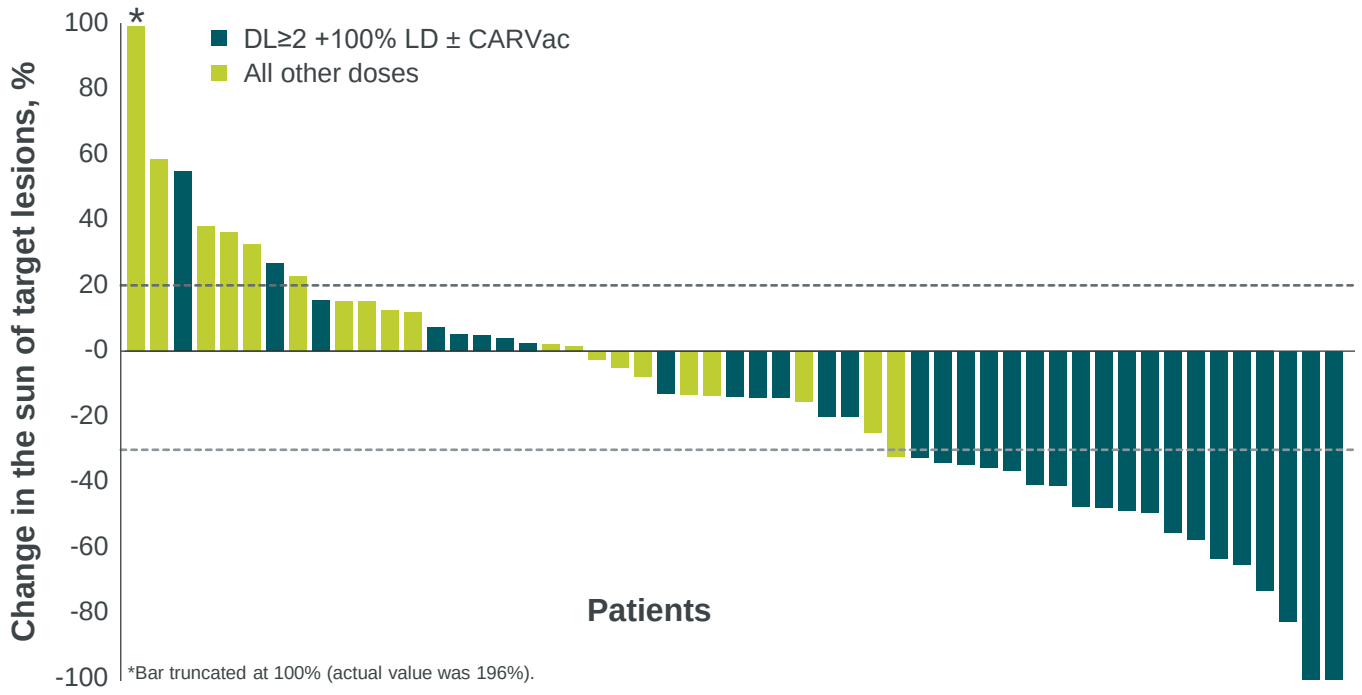
ACT = adoptive cell transfer; AE = adverse event; CAR = chimeric antigen receptor; CARVac = CAR T-cell amplifying RNA vaccine; CLDN6 = claudin-6; CRS = cytokine release syndrome; Cy = cyclophosphamide; DL = dose level; Flu = fludarabine; HLH = hemophagocytic lymphohistiocytosis; ICANS = immune effector cell-associated neurotoxicity syndrome; IEC-HS = immune effector cell-associated HLH-like syndrome; LD = lymphodepletion.

ESMO 2024 | John Haanen , et. al., Safety and efficacy of BNT211-01 in r/r CLDN6+ solid tumors (NCT04503278), Presentation 611O

BNT211-01: Best Overall Response

Among the 41 patients who received CAR T dose level 2 or dose level 3 (with or without CARvac) - shown below in dark green - ORR and DCR were 51.5% and 84.8%, respectively

Best overall response per RECIST v1.1



Response[a]	Total (N=74)[b]
Evaluable patients, n	64
ORR, n (%)	**21 (32.8)**
95% CI (%)	18.5–40.1
CR, n (%)	3 (4.1)
PR, n (%)	18 (24.3)
DCR, n (%)	**43 (67.2)**
95% CI (%)	46.1–69.5

Response[a]	DL≥2 +100% LD ± CARVac (N=41)[b,c]
Evaluable patients, n	33
ORR, n (%)	**17 (51.5)**
95% CI (%)	26.3–57.9
DCR, n (%)	**28 (84.8)**
95% CI (%)	51.9–81.9

Data cut-off: May 16, 2024.

[a] Includes tumor marker responses; [b] Excludes patients who received an out-of-specification product; [c] DL2=1×10^8; DL3=2–5×10^8 CAR T cells.
ACT = adoptive cell transfer; CAR = chimeric antigen receptor; CARVac = CAR T-cell amplifying RNA vaccine; CI =confidence interval; CR = complete response; DCR = disease control rate; DL = dose level; LD = lymphodepletion; ORR = objective response rate; PR = partial response.

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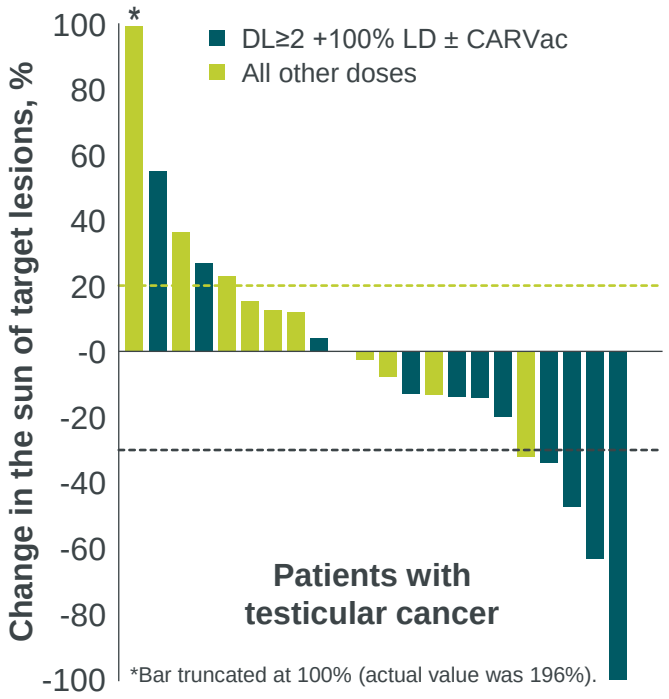
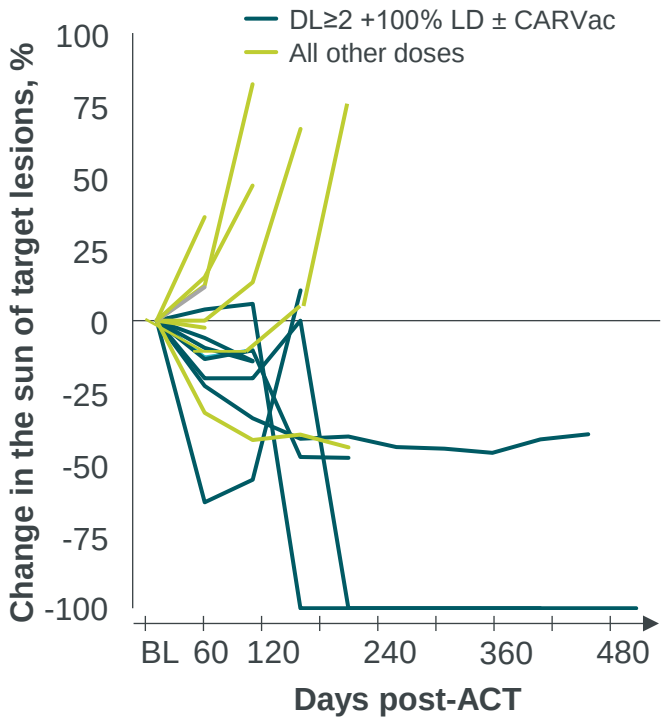
BNT211-01: Overall Response Rate – Testicular Cancer

In this patient group, overall response rate was 24%; at DL2 and DL3 ORR was 41.7%. Two patients had a surgical complete response that lasted for over a year

Best overall response per RECIST v1.1



Response over time



Response[a]	Total (N=27)[b]
Evaluable patients, n	25
ORR, n (%)	**6 (24.0)**
95% CI (%)	8.6–42.3
DCR, n (%)	**14 (56.0)**
95% CI (%)	32.0–71.3

Response[a]	DL≥2 +100% LD ± CARVac (N=14)[b,c]
Evaluable patients, n	12
ORR, n (%)	**5 (41.7)**
95% CI (%)	12.8–64.9
DCR, n (%)	**9 (75.0)**
95% CI (%)	35.1–87.2

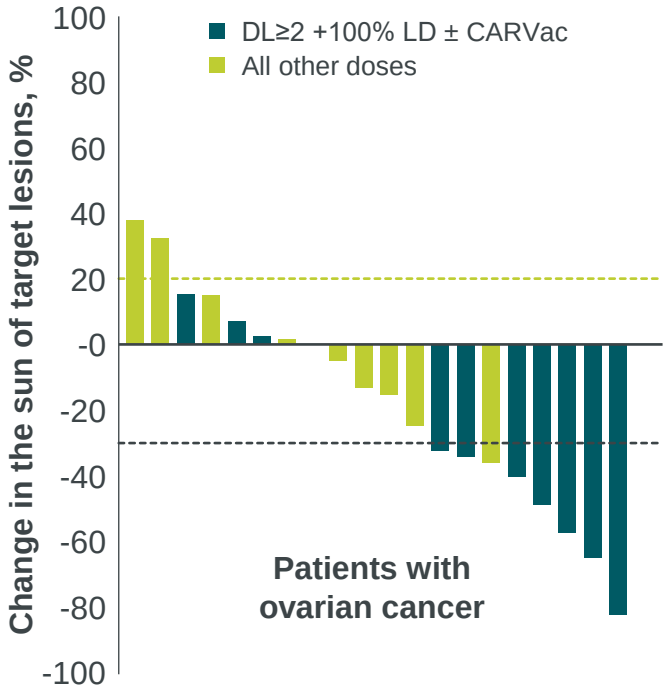
Data cut-off: May 16, 2024.

a. Includes tumor marker responses; b. Excludes patients who received an out-of-specification product; c. DL2=1×10^8; DL3=2–5×10^8 CAR T cells.
ACT = adoptive cell transfer; BL = baseline; CAR = chimeric antigen receptor; CARVac = CAR T-cell amplifying RNA vaccine; CI =confidence interval; DCR = disease control rate; DL = dose level; LD = lymphodepletion; ORR = objective response rate.

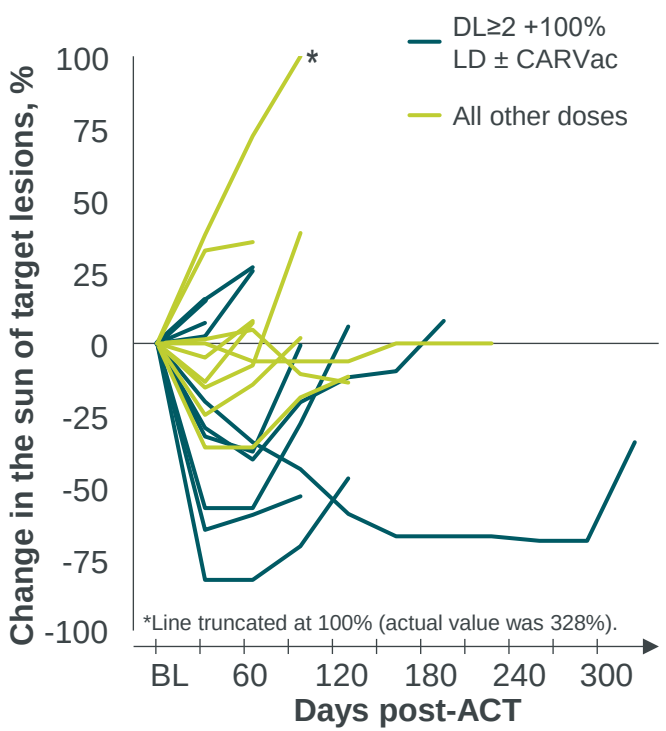
BNT211-01: Overall Response Rate – Ovarian Cancer

Of the 24 evaluable patients across all DLs we see ORR was 33.3% while DCR was 75% - the same parameters when considered for DL2 and above are 58.3% and 83.3% respectively

Best overall response per RECIST v1.1



Response over time



Response[a]	Total (N=30)[b]
Evaluable patients, n	24
ORR, n (%)	**8 (33.3)**
95% CI (%)	12.3–45.9
DCR, n (%)	**18 (75.0)**
95% CI (%)	40.6–77.3

Response[a]	DL≥2 +100% LD ± CARVac (N=16)[b,c]
Evaluable patients, n	12
ORR, n (%)	**7 (58.3)**
95% CI (%)	19.8–70.1
DCR, n (%)	**10 (83.3)**
95% CI (%)	35.4–84.8

Data cut-off: May 16, 2024.

a. Includes tumor marker responses; b. Excludes patients who received an out-of-specification product; c. DL2=1×10^8; DL3=2–5×10^8 CAR T cells.
ACT = adoptive cell transfer; BL = baseline; CAR = chimeric antigen receptor; CARVac = CAR T-cell amplifying RNA vaccine; CI =confidence interval; DCR = disease control rate; DL = dose level; LD = lymphodepletion; ORR = objective response rate.

ESMO 2024 | John Haanen , et. al., Safety and efficacy of BNT211-01 in r/r CLDN6+ solid tumors (NCT04503278), Presentation 611O

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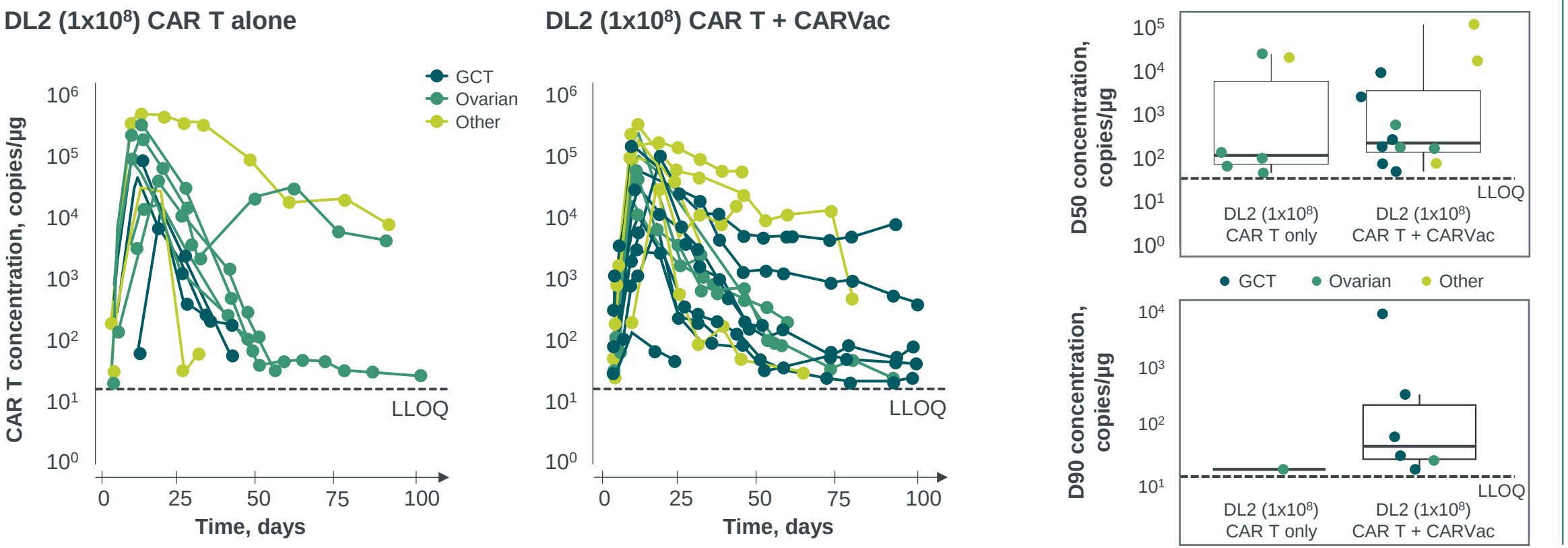
BNT211-01: At DL2, CARVac Improved CAR T Persistence Beyond 100 Days

Adding CARVac limits the decline and induces a plateau of CAR-T cells with robust and ongoing detection for several additional weeks in nearly all patients who received DL2+CARVac



Data cut-off: May 16, 2024.

CAR = chimeric antigen receptor; CARVac = CAR T-cell amplifying RNA vaccine; CI =confidence interval; CLDN6 = claudin 6; DL = dose level; GCT = germ cell tumor.

ESMO 2024 | John Haanen , et. al., Safety and efficacy of BNT211-01 in r/r CLDN6+ solid tumors (NCT04503278), Presentation 611O

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BNT211 – ESMO 2024 Data: Key Takeaway Messages

Safety Profile:

The safety profile of the investigational therapy CLDN6 CAR T cells ± CARVac was consistent with the previously published effect of CAR T therapies;[1–3] repeated CARVac administration did not result in increased toxicity

Efficacy:

Encouraging signs of antitumor activity across all indications, especially in patients with germ cell tumors/ testicular cancer and ovarian cancer:

- Among patients who received DL≥2 +100% LD ± CARVac, ORR[a] was 41.7% (testicular) and 58.3% (ovarian)
- Three patients experienced durable responses that lasted over a year (2 CRs, 1 PR)

CARVac improved CAR T persistence beyond 100 days

Outlook:

Follow up is ongoing. The study will evaluate the safety and tolerability of DL3 + CARVac

1. Shah NN, et al. J Clin Oncol 2020; 38(17):1938–1950; 2. Hines MR, et al. Br J Haematol 2021;194(4):701–707; 3. Liechtenstein DA, et al. Blood 2021;138(24):2469–2484; Hines MR, et al. Transplant Cell Ther 2023;29(7):438.e1–438.e16.
a. Includes tumor marker responses; DL2=1×10^8; DL3=$2–5\times10^8$ CAR T cells.
CAR = chimeric antigen receptor; CARVac = CAR T-cell amplifying RNA vaccine; CR = complete response; DCR = disease control rate; DL = dose level; LD = lymphodepletion; ORR = objective response rate; PR = partial response.

ESMO 2024 | John Haanen , et. al., Safety and efficacy of BNT211-01 in r/r CLDN6+ solid tumors (NCT04503278), Presentation 611O

8[1]

BNT323 / DB-1303[1]

HER2-low Breast Cancer

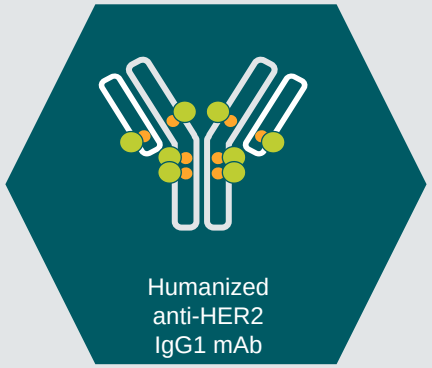
DYNASTY-Breast02: A Phase 3 trial of BNT323/DB-1303 vs Investigator's Choice Chemotherapy in HER2-low, Hormone Receptor Positive, Metastatic Breast Cancer

Joyce O'Shaughnessy (Baylor University Medical Center, Texas Oncology, US Oncology Dallas, TX, USA) et al.; Presentation Number: 436TiP

1. Partnered with Duality Biologics

BIONTECH

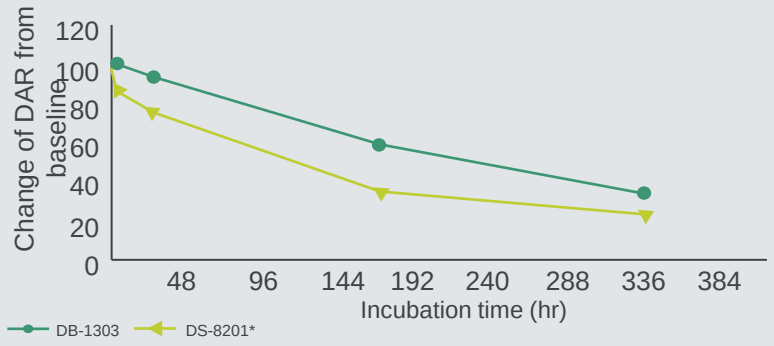
BNT323/DB-1303[1]: A HER2 ADC with a Potentially Differentiated Profile



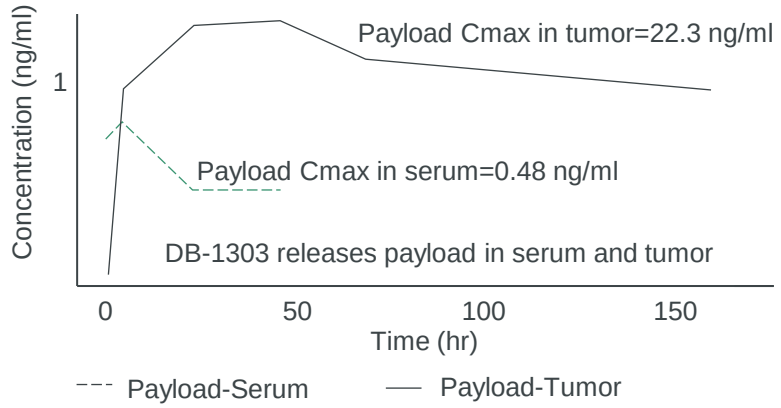
- A humanized anti-HER2 IgG1 mAb, with a wild-type Fc
- A proprietary DNA topoisomerase I inhibitor (P1003)
- A maleimide tetrapeptide-based tumor-selectively cleavable linker (L101)
- High drug-to-antibody ratio: ~8

Lin S. et al. Abstract #252. Presented at EORTC-NCI-AACR in 2022.

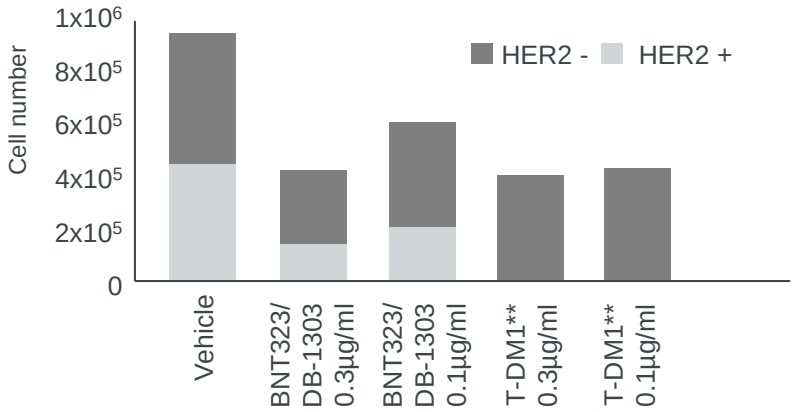
Superior *in vitro* plasma stability in human plasma



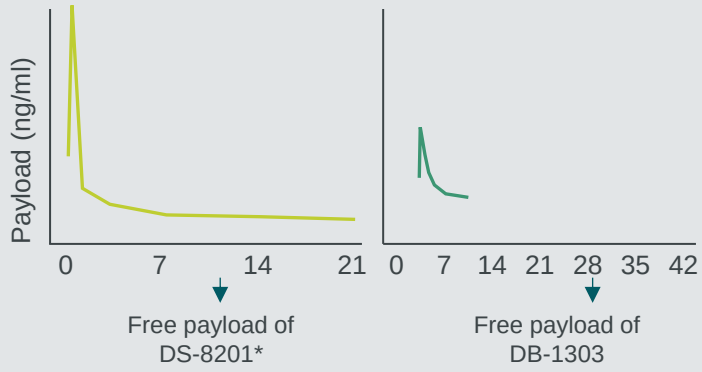
Sustained tumor-selective drug release in tumor-bearing mice



Efficient bystander killing in tumor cell lines



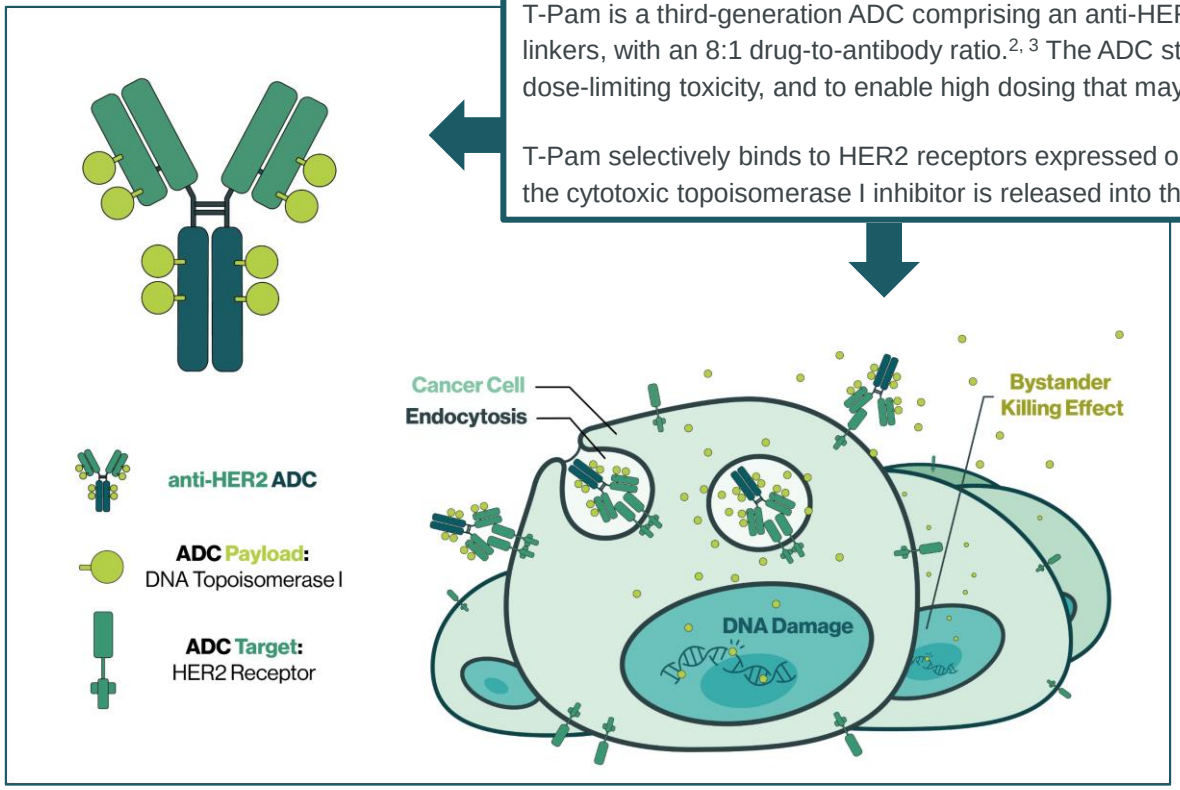
Rapid systemic clearance in monkeys



.1.Partnered with DualityBio. *DS-8201 is an in-house produced analog of DS-8201, Trastuzumab deruxtecan; **Trastuzumab-Emtansin.
ADC = Antibody-drug conjugate; cmax = maximum concentration; DAR = Drug antibody ratio. HER = human epidermal growth factor receptor.

BNT323/DB-1303[1] Proposed Mechanism of Action

A humanized anti-HER2 IgG1 monoclonal antibody, conjugated to a DNA topoisomerase I inhibitor via a cathepsin-cleavable maleimide tetrapeptide (GGFG) linker with a drug-to-antibody ratio of ~8:1[2,3]



T-Pam is a third-generation ADC comprising an anti-HER2 monoclonal antibody connected to a proprietary topoisomerase-1 inhibitor via cleavable linkers, with an 8:1 drug-to-antibody ratio.[2, 3] The ADC stability is designed to reduce off-target effects that typically result in adverse reactions and dose-limiting toxicity, and to enable high dosing that may enhance the potential for therapeutic effectiveness in tumors with HER2+ low expression.

T-Pam selectively binds to HER2 receptors expressed on HER2-low breast cancer cells.[4] Upon endocytosis and cleavage by a lysosomal enzyme, the cytotoxic topoisomerase I inhibitor is released into the breast cancer cell, resulting in DNA damage and apoptotic cell death.[4]

Background and rationale

- Traditional binary distinction of HER2-positive and HER2-negative breast cancer based on immunohistochemical score overlooks a spectrum of HER2 expression.[5]
- Currently, patients with HR+, HER2-low advanced or metastatic breast cancer follow the same treatment paradigm as those with HR+, HER2-negative breast cancer: endocrine therapy (ET) with a cyclin dependent kinase (CDK) 4/6 inhibitor as first line therapy.[6,7, 8] Opportunity exists to improve outcomes in the HER2-low population.
- Preclinically, BNT323/DB-1303[1] displays potent antitumor activity in HER2-positive and HER2-low tumor models. The phase 1 trial (NCT05150691) showed promising antitumor responses in HER2-low breast cancer (unconfirmed ORR 38.5%, n=5/13) alongside a favorable toxicity profile across 85 patients with advanced/metastatic solid tumors, with no dose limiting toxicities observed up to 10 mg/kg.[3]

1. Partnered with Duality Bio; 2. Lin S, et al. Eur J Cancer. 2022; 174, S91. doi: https://doi.org/10.1016/S0959-8049(22)01039-5; 3. Moore K, et al. J Clin Oncol 41, 2023; suppl 16; abstr 3023. doi; https://doi.org/10.1200/JCO.2023.41.16_suppl.3023; 4. Metrangolo V, Engelholm LH. 2024; 16(2):447. doi: https://doi.org/10.3390/cancers16020447; 5. Molinelli Cet al., ESMO Open. 2023 Aug;8(4):101592. doi: 10.1016/j.esmoop.2023.101592; 6. Gennari A et al., Ann Oncol. 2021; 32: 1475–1495; **7.** Gradishar WJ et al., J Natl Compr Cancer Netw. 2022; 20: 691–722; 8. Wang X. et al. Cancer Gene Ther 2024. https://doi.org/10.1038/s41417-024-00747-x. ADC = antibody drug conjugate; HER2 = human epidermal growth factor receptor 2; HR = hormone receptor; ORR = overall response rate.

BIONTECH

BNT323/DB-1303[1] Phase 3 Trial in CTx-Naïve Patients with HR+/HER2-Low Breast Cancer who progressed after 2 ET therapies (DYNASTY-Breast02)

Phase 3, randomized, multi-center, open-label study of BNT323/DB-1303[1] (trastuzumab pamirtecan) versus investigator's choice chemotherapy in HER2-Low, HR+ metastatic breast cancer (NCT06018337)

Eligibility criteria

- Adult aged 18 years and older
- Documented advanced or metastatic HR+/HER2-low (IHC 1+ or IHC 2+/ISH-) breast cancer
- Progressed on at least 2 lines of prior ET or within 6 months of first line ET + CDK4/6 inhibitor in the metastatic setting
- No prior chemotherapy or HER2-therapy for advanced or metastatic breast cancer*
- ECOG 0-1

Stratification factors

- Prior CDK4/6 inhibitor use, HER2 IHC expression, prior taxane use in the non-metastatic setting

N=532 (Estimated)

R 1:1

BNT323/DB-1303[1], 8mg/kg IV, Q3W

Investigator's choice

Capecitabine, 1000 or 1250 mg/m^2 BID orally for 2 weeks Q3W
or
Paclitaxel, 80 mg/m^2 IV infusion QW
or
Nab-paclitaxel, 100 mg/m^2 IV infusion QW for 3 weeks Q4W

Endpoints

Primary: PFS by BICR according to RECIST 1.1

Secondary: OS, ORR, DoR, DCR, TEAEs and SAEs, PRO, PK

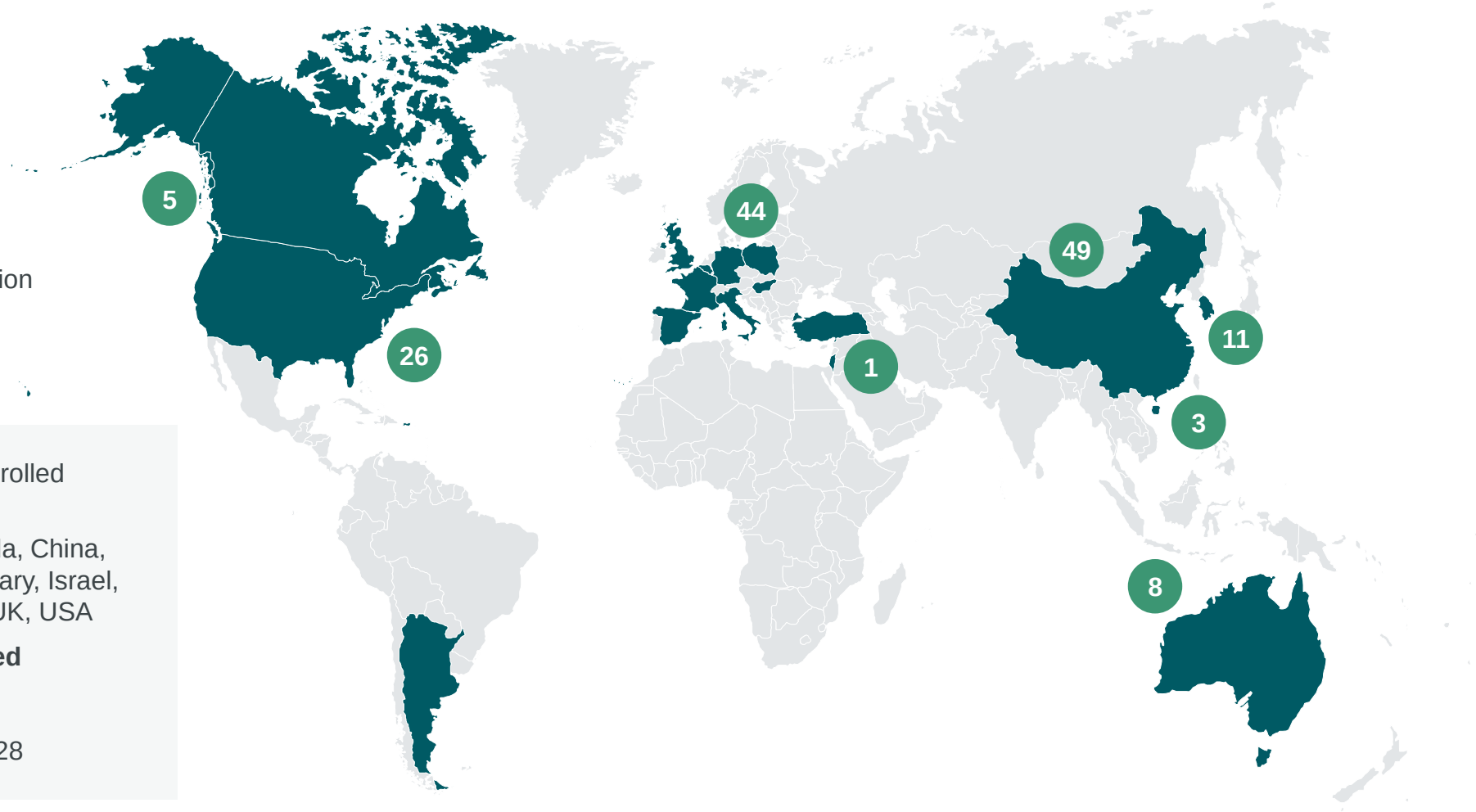
Exploratory: PK, ADA prevalence and incidence, DCR, TTR, PFS2, TFST, TSST, Patient-reported treatment tolerability

1. Partnered with DualityBio; 2. Gennari A et al., Ann Oncol. 2021; 32: 1475– 1495. * Subjects who have received chemotherapy in the neo-adj. or adj. setting are eligible, as long as they have had a disease-free interval (defined as completion of systemic chemotherapy to diagnosis of adv. or met disease) of >12 months. ADA = antibody drug antibody; CTx = chemotherapy; DCR = disease control rate; DoR = duration of response; HR = hormone receptor; ECOG = eastern Cooperative oncology group; ET = endocrine therapy; HER = human epidermal growth factor; IV = intravenous; ORR = objective response rate; OS = overall survival; PFS = progression free survival; PK = pharmacokinetics; PRO = patient reported outcome; QXW = every X weeks; RECIST = response evaluation criteria in solid tumors; SAE = severe adverse event TTR = time to response; TF/SST = time to first/second subsequent treatment or death.

BNT323/DB-1303[1] Evaluated in a Global, Multi-Center, Phase 3 Trial (DYNASTY-Breast02)

Planned study sites

- Countries with planned sites
- Number of initiated sites in each region (correct at time of print)



Approximately 532 patients will be enrolled across the following countries:

- Argentina, Australia, Belgium, Canada, China, France, Germany, Hong Kong, Hungary, Israel, Italy, Korea, Poland, Spain, Turkey, UK, USA
- A total of **147 sites currently initiated**

First patient in: January 2024
Estimated study completion: May 2028

1. Partnered with DualityBio;

ESMO 2024 | Joyce O'Shaughnessy, et. al., Phase 3 trial of BNT323/DB-1303 in HER2-low, HR+, mBC (NCT06018337), Poster 436TiP

BIONTECH

1

9

BNT314 / GEN1059[1]

Malignant Solid Tumors

Phase 1/2 dose escalation/expansion trial to evaluate safety and preliminary efficacy of DuoBody-EpCAMx4-1BB (BNT314/GEN1059) alone or in combination with an immune checkpoint inhibitor in patients with malignant solid tumors

I. Melero , Presentation Number: 1072TiP

1. Partnered with Genmab

BIONTECH

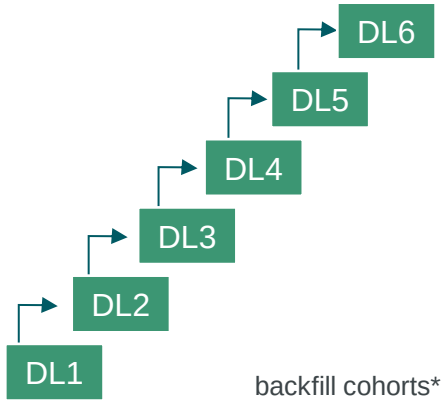
BNT314/GEN1059[1] as Monotherapy or in Combination with Immune Checkpoint Inhibitor in Patients with Malignant Solid Tumors

Phase 1/2, FIH, open-label, dose escalation and expansion trial to evaluate safety of BNT314/GEN1059[1] alone or in combination with pembrolizumab in patients with different types of cancer (NCT06150183)

Eligibility

- Histologically confirmed, advanced solid tumors
- Disease progression after standard therapy
- Measurable disease per RECIST v1.1
- ECOG PS 0–1

Monotherapy



backfill cohorts*

Combination Therapy
Safety run-in

BNT314/GEN1059[1]
i.v.
+ **pembrolizumab**, i.v

Combination therapy

BNT314/GEN1059[1] i.v.
+
pembrolizumab i.v.

For 2L+ selected advanced solid tumor patients

* Additional cohorts assign patients to specific DLs, based on emerging safety, PK, and PD data to support BNT314 dose optimization

Key endpoints

	Dose escalation	SRI	Expansion
Primary:	DLT, Safety, MTD/MAD/RP2D	DLT, safety, tolerability	ORR
Secondary:	PK, DCR, ORR, DOR	DCR, ORR, DOR, PFS, OS	DCR, DOR, PFS, OS, safety, PK

Status
Recruiting

1. Partnered with Genmab;. ADA = anti-drug antibody; DCR = disease control rate; DL = dose level; DLT = dose limiting toxicity; DOR = duration of response; ECOG = Eastern Cooperative Oncology Group; FIH = first in human; iMAD = maximal administered dose; MTD, maximal tolerated dose; ORR = objective response rate; OS = overall survival; PFS = progression free survival; PK = pharmacokinetics; RECIST = Response Evaluation Criteria in Solid Tumors; RP2D = recommended phase 2 dose; TEAEs = treatment emergent adverse events.

ESMO 2024 | I. Melero , et. al., Phase 1/2 trial of BNT314/GEN1059 in malignant solid tumors, (NCT06150183), Poster 1072TiP

BNT314/GEN1059[1]: Proposed Mechanism of Action

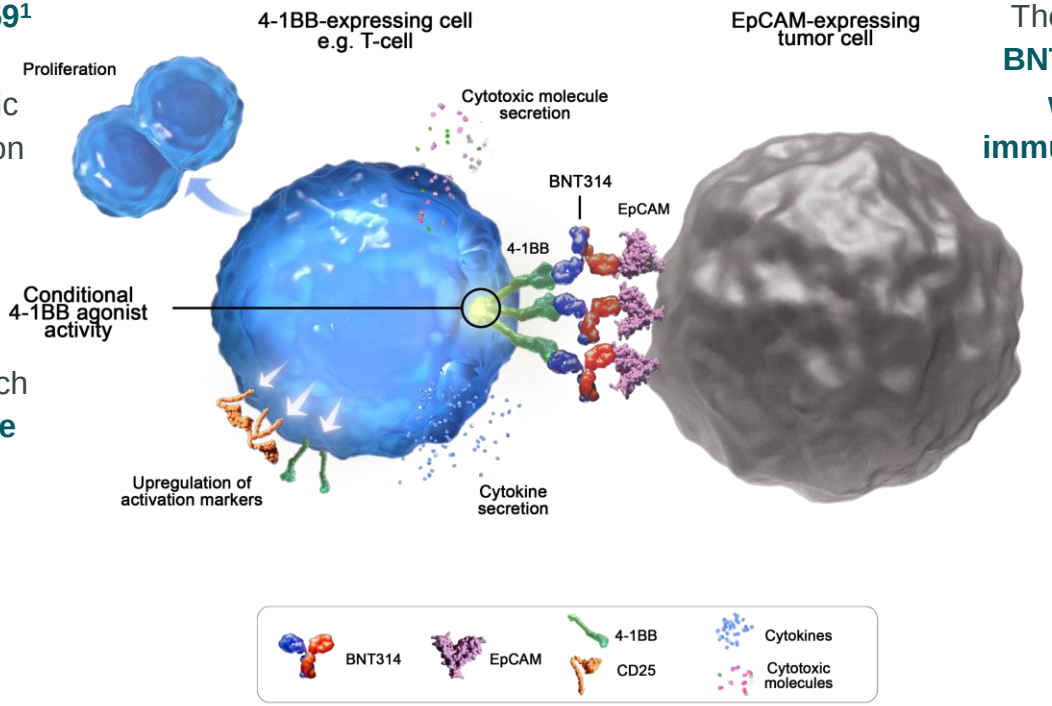
BNT314/GEN1059[1] (DuoBody-EpCAM×4-1BB) is an investigational bispecific antibody designed to enhance T-cell activation in the tumor microenvironment by targeting 4-1BB and EpCAM.

Background and rationale

- While PD-(L)1 inhibitors have marked an advancement in immuno-oncology, the response to such treatments varies among patients, and not all responders sustain long-term benefits, highlighting an ongoing unmet medical need in patients with advanced solid tumors[2,3]. Furthermore, the therapeutic potential of 4-1BB agonists has been recognized in immuno-oncology[4-6].
- Preclinical studies showed that BNT314/GEN1059[1] conditionally enhanced activation and proliferation of T cells, cytokine secretion, and cytotoxic activity. Furthermore, proof-of-principle studies showed antitumor activity of an Fc-silent EpCAMx4-1BB bispecific antibody in mice[7].

BNT314/GEN1059[1] is Fc-silenced. Its 4-1BB agonistic activity depends on **simultaneous binding to EpCAM**.

This conditional activation approach aims to **potentiate the immune response** at the tumor site, while **minimizing systemic exposure**.



The combination of **BNT314/GEN1059[1] with** established **immune checkpoint inhibitors** like pembrolizumab is hypothesized to **amplify antitumor immunity**.

1. Partnered with Genmab; 2. Galon, J. and D. Bruni, Nat Rev Drug Discov, 2019. 18(3); 3. Jenkins, R.W., D.A. Barbie, and K.T. Flaherty, Br J Cancer, 2018. 118(1); 4. Chester, C., et al., Blood, 2018. 131(1); 5. Kim, A.M.J., M.R. Nemeth, and S.-O. Lim, Frontiers in Oncology, 2022. 12; 6. Melero, I., et al., Cancer Discovery, 2023. 13(3); 7. Fellermeier-Kopf, S., et al., 1072P. Annals of Oncology, 2023. 34
CD25 = cluster of differentiation 25; EpCAM = epithelial cell adhesion molecule; Fc = tail region of an antibody that interacts with cell surface receptors (e.g. 4-1BB or EpCAM); PD-L1 = programmed cell death ligand 1;

ESMO 2024 | I. Melero , et. al., Phase 1/2 trial of BNT314/GEN1059 in malignant solid tumors, (NCT06150183), Poster 1072TiP

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BNT314/GEN1059[1] Evaluated in a Global, Multi-Center, Phase I/II Trial

Active and planned study sites

- Active sites
- Planned sites*

* Additional countries to be included for the expansion part

Approximately 360 patients will be enrolled across the following countries:

- Belgium, Spain, United Kingdom, USA as well as additional countries to be included such as Japan and Denmark.

First patient in: Jan 2024

1. Partnered with Genmab.

ESMO 2024 | I. Melero , et. al., Phase 1/2 trial of BNT314/GEN1059 in malignant solid tumors, (NCT06150183), Poster 1072TiP

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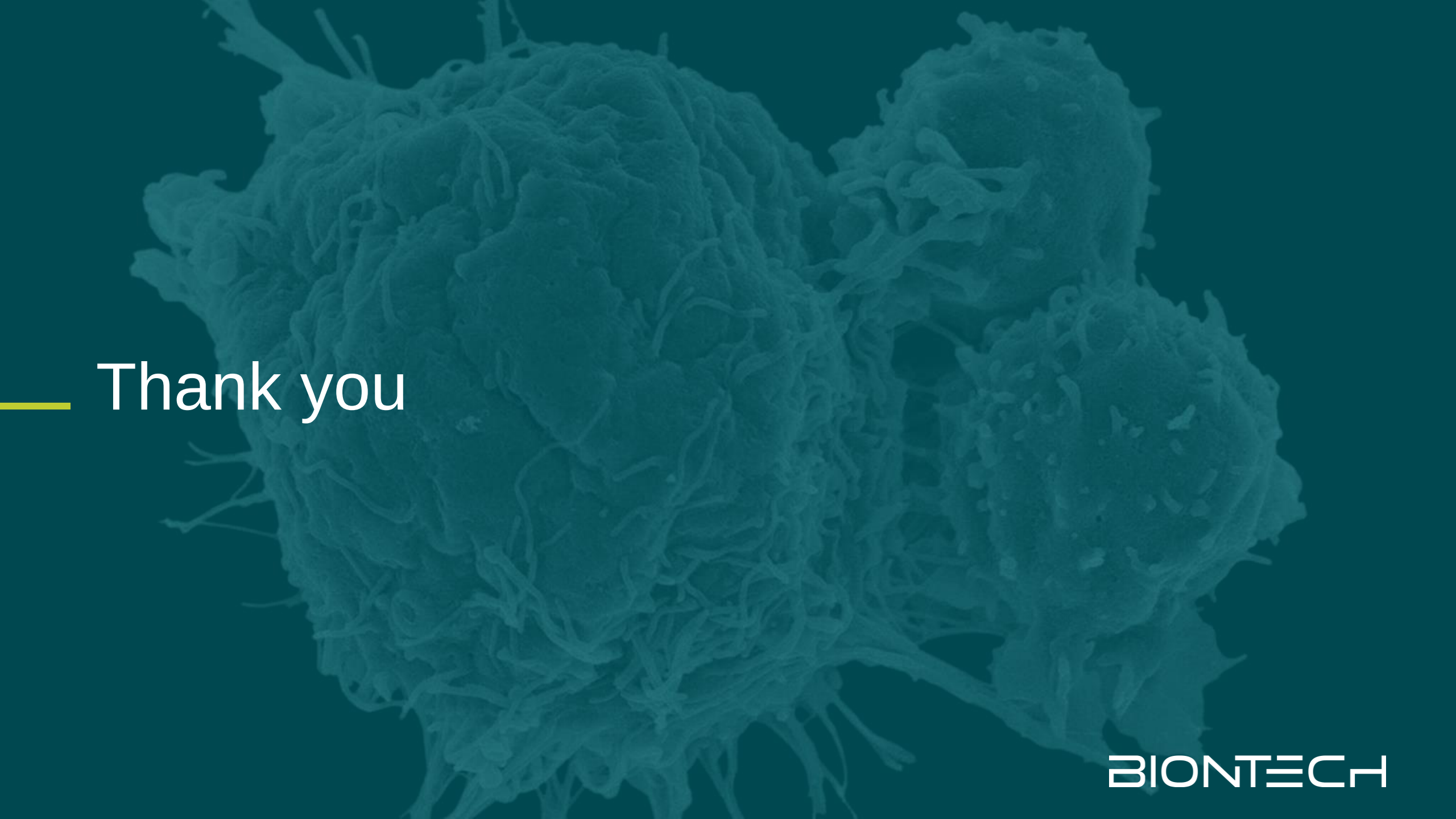

Thank you

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