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## **Best of Oncology**



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> DGHO/OEGHO/SGH/SMO Basel 2024





### **Disclosures**

- Sponsorship or research funding: Ariad, Pfizer, Novartis, BMS, Roche, AOP, MSD
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## Excellence in oncology is interdisciplinary and interprofessional



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## Communication and Cooperation



## To improve future therapies!



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Prevention

## The basis for innovation is science: pioneers in immunology



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2019 Albert Lasker Basic Medical Research Award, which has been given to Max Dale Cooper and Jacques Miller.

Germain R, NEJM 2019

### "Hallmarks of Cancer" – the pic for the fridge



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# Some of my personal favorite concepts in oncology



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- 1. BiTEs, CARTs and vaccines in oncology: paradigm-shift in the treatment of solid cancer?
- 2. There is still news from classical immune checkpoints
- 3. What about targeted compounds?
- 4. ADCs a revival of chemotherapy but targeted
- 5. Liquid biopsy for therapy tailoring
- 6. Targeting cancer cachexia



Very personal view

## **BNT211-01 trial: principle**



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CLDN6 is an oncofetal antigen, expressed during fetal organogenesis and overexpressed in many solid tumors yet absent in healthy adult tissues<sup>1</sup>

 BNT211 is an investigational candidate combining CLDN6-targeted CAR T<sup>1,2</sup> and CARVac<sup>3,4</sup>

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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. APC, antigen-presenting cell; CAR, chimeric antigen receptor; CLDN6, claudin-6; IV, intravenous.



Mackensen et al., Nat Med 2023 Hanen et al., ESMO 2024



### BNT211-01 trial design: Best overall response rates (ORR)



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## **Targeting DLL-3 by TCE in SCLC**



50

45

40-

35-

30-

25-

20-

15

10-

5 -

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2001

2004

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17

2013

2016



Howlader et al, NEJM 2020

2007

2010

Women



## DeLLphi(n)-301: Tarlatamab is a good jump forward

PFS/OS after Chemo (IO) plus second line therapy





Characteristic	Tarlatamab, 10 mg		Tarlatamab, 100 mg	
	Parts 1 and 2 (N=100)	Part 3 (N=34)	Part 1 (N=88)	
No. of previous lines of therapy — no. (%)				
1	2 (2)	0	2 (2)	
2	65 (65)	22 (65)	48 (55)	
3	19 (19)	6 (18)	22 (25)	
>3	14 (14)	6 (18)	16 (18)	
Median no. of previous lines of therapy (range)	2.0 (1-6)	2.0 (2-6)	2.0 (1-8)	









#### Pons-Tostvint et al, Lung Cancer 2024



### **DeLLphi: Tarlatamab induces long**term disease control in some patients



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Dowlati et al, J Clin Oncol 2024



Duration of Treatment (wk)

### Phase 2 (responder)

### **ADRIATIC: PD-L1 blockade improves** OS in LD-SCLC



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Table 2. Objective Responses	(Intention-to-Treat	Population).*
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End Point	Durvalumab (N = 264)	Placebo (N = 266)
Median duration of response (95% CI) — mo $\P$	33.0 (22.4–NR)	27.7 (9.6–NR)
Ongoing response at 12 mo (95% CI) — % $\P$	74 (59–84)	60 (44–73)
Ongoing response at 18 mo (95% CI) — %¶	71 (57–82)	55 (39–68)



### LAURA: TKI-maintenance after **RCT is new SOC**



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#### Lu et al, NEJM 2024









#### Genotype-Directed Therapies FDA-Approved in NSCLC\*

### **Targeting cancer by ADCs**



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## OptiTROP-Breast01: Sac-TMT improves OS in r/r TNBC



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## DESTINY-Breast12: Trastuzumab-DXT has excellent CNS activity in r/r Her2/neu+ BC

DESTINY



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Harbeck et al, Nat Med 2024

## Neo-COAST 02: ADC (Dato-DXT) going to the perioperative setting in NSCLC



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92.2%

92.1%

**95.8%** 

**SURGERY RATES** 

Dascone et al, WCLC 2024

## GALAXY: ctDNA clearance and curative potential in stage II-IV CRC



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Characteristic	No. of patients (%)	Characteristic	No. of patients (%)
Median age in years (range)	• 69 (28–95)	Median follow-up in months (range)	23 (2-49)
Sex Male Female	1,149 (51%) 1,091 (49%)	Neoadjuvant treatment Neoadjuvant chemotherapy None (upfront surgery)	218 (10%) 2,022 (90%)
ECOG score 0 1	2,046 (91%) 194 (9%)	Adjuvant treatment Adjuvant chemotherapy Observation	946 (42%) 1,294 (58%)
Tumor location Right-sided colon Left-sided colon	863 (39%) 1,377 (61%)	BRAF mutation status BRAF WT BRAF V600E	2,062 (92%) 178 (8%)
Pathological T stage T1–T2 T3–T4 Unknown	317 (14%) 1,630 (73%) 293 (13%)	RAS mutation status RAS WT RAS mut	1,303 (58%) 937 (42%)
Pathological N stage NO N1-N2 Unknown	922 (41%) 1,025 (46%) 293 (13%)	MSI status MSS or MSI low MSI high	2,025 (90) 215 (10%)
Pathological stage I II III IV	234 (10%) 652 (29%) 936 (42%) 418 (19%)	Radiological recurrence Yes No	500 (22%) 1,740 (78%)



Interim analysis n=2240 Median follow-up 23 months

Nakamura et al, Nat Med 2024

## GALAXY: ctDNA clearance and curative potential in stage II-IV CRC



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## GALAXY: ctDNA clearance by ACT in MRD+ pts is linked to superior outcome





Nakamura et al, Nat Med 2024

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## GDF-15 is central for progressive cancer cachexia and can be targeted in mice



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Treatment with a GDF15 neutralizing monoclonal antibody alleviates weight loss and improves muscle function and performance

## The concept of GDF-15 inhibition also works in cancer cachexia in humans

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Characteristic	Placebo (N = 45)	Ponsegromab, 100 mg (N=46)	Ponsegromab, 200 mg (N=46)	Ponsegromab, 400 mg (N = 50)	All Patients (N=187)
Madian and (IOD)	(	72	(	(	(
wedian age (iQit) — yi	(57–71)	(64–76)	(60–72)	(60-72)	(60–74)
Female sex — no. (%)	17 (38)	19 (41)	15 (33)	18 (36)	69 (37)
Race — no. %†					
White	26 (58)	27 (59)	28 (61)	35 (70)	116 (62)
Asian	18 (40)	19 (41)	18 (39)	15 (30)	70 (37)
Not reported	1 (2)	0	0	0	1 (1)
Median weight (IQR) — kg	53.8 (46.0–58.4)	50.2 (43.4–61.2)	55.2 (47.0–69.5)	58.1 (50.9–67.4)	54.8 (46.0–63.8)
Body-mass index					
Median (IQR)	19.0 (17.2–21.3)	19.3 (17.5–21.2)	20.6 (17.7–24.1)	20.5 (19.2–22.8)	19.8 (17.6–22.3)
<20 — no. (%)	30 (67)	28 (61)	22 (48)	19 (38)	99 (53)
Percent weight loss during 6 mo be- fore screening — no. (%)					
<5%	6 (13)	10 (22)	9 (20)	5 (10)	30 (16)
5 to <10%	21 (47)	15 (33)	12 (26)	21 (42)	69 (37)
≥10%	18 (40)	21 (46)	25 (54)	24 (48)	88 (47)
BMI-adjusted weight-loss category‡					
No. of patients (%)					
Category 1	0	0	1 (2)	1 (2)	2 (1)
Category 2	0	6 (13)	3 (7)	5 (10)	14 (7)
Category 3	15 (33)	18 (39)	24 (52)	20 (40)	77 (41)
Category 4	30 (67)	22 (48)	18 (39)	24 (48)	94 (50)
Median category (IQR)	4 (3-4)	3 (3-4)	3 (3-4)	3 (3-4)	4 (3-4)
Cancer type — no. (%)					
Non-small-cell lung	15 (33)	17 (37)	21 (46)	21 (42)	74 (40)
Pancreatic	14 (31)	16 (35)	15 (33)	14 (28)	59 (32)
Colorectal	16 (36)	13 (28)	10 (22)	15 (30)	54 (29)
Cancer stage — no. (%)					
1	0	1 (2)	0	1 (2)	2 (1)
П	3 (7)	5 (11)	4 (9)	2 (4)	14 (7)
111	12 (27)	10 (22)	8 (17)	4 (8)	34 (18)
IV	30 (67)	30 (65)	34 (74)	43 (86)	137 (73)



Klinisch und akademisch relevant, aktuelle klinische Bedeutung aber unklar (OS? QoL?)!

### And many more...



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- ESOPEC (resectable EC FLOT >> CROSS)
- TOPGEAR (periop RCHT = CHT in resectable GC)
- NICHE-3 (Nivo/Relatlimab MSI neadj CRC)
- POD1UM-303/InterAACT 2 (Retifanlimab/CHT >> CHT in mRC)
- COLLISSION (hep. Meta CRC RFA = surgery)
- TransMet (Hep. Tx in unres. liver only CRC-meta)
- MARIPOSA-2 (Amiv.+Chemo in Osi-res NSCLC)
- NADINA (neoadj Nivo/Ipi >> adj. Nivo in res. MM)
- Tropion-Lung01 (Dato-Dxt >> Docetaxel in NSCLC)
- CABINET (Cabozantinib in NET)

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### **THANK YOU!**



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