Society for Immunotherapy of Cancer

Advances in Cancer Immunotherapy™

Trials of Emerging Agents, Combinations and Disease Settings

Arndt Vogel

Medical School Hannover

Germany

Disclosures

- Consulting Fees:

  Amgen, Roche, Bayer, Sanofi, BMS, Lilly, Novartis, EISAI, AstraZeneca, Merck, Incyte, Ipsen, PierreFabre, MSD, Sirtex, BTG, Servier, Terumo.

- I will be discussing non-FDA approved indications during my presentation.

Trials of Emerging Agents, Combinations and Disease Settings

Neoadjuvant setting
- CRC: NICHE
- HCC: Cabo-Atzeo

Adjuvant setting
- HCC: Early and intermediate stage

Per-operative setting
- GC: DANTE

IO combinations with Chemo
- CCC: TOPAZ-1

IO combinations with targeted therapies
- GC: KEYNOTE-811/INTEGA

Chemo priming prior IO
- CRC: MAYA

CAR-T cells
- GC

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ARTICLES
https://doi.org/10.1038/s41591-020-0805-8
nature medicine
Check for updates

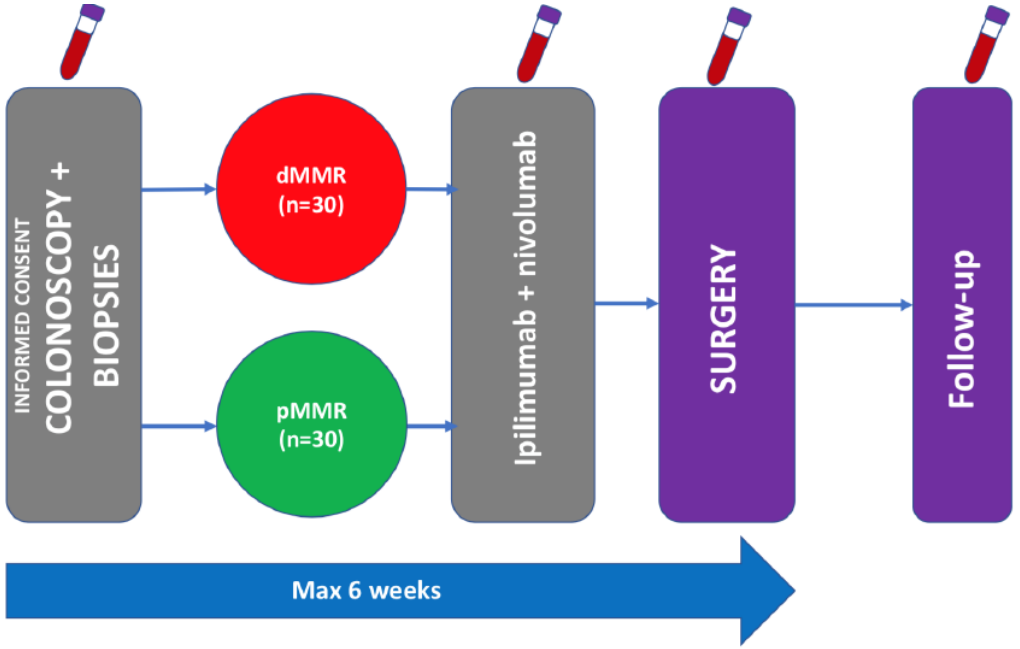
Neoadjuvant immunotherapy leads to pathological responses in MMR-proficient and MMR-deficient early-stage colon cancers

Primary objective:

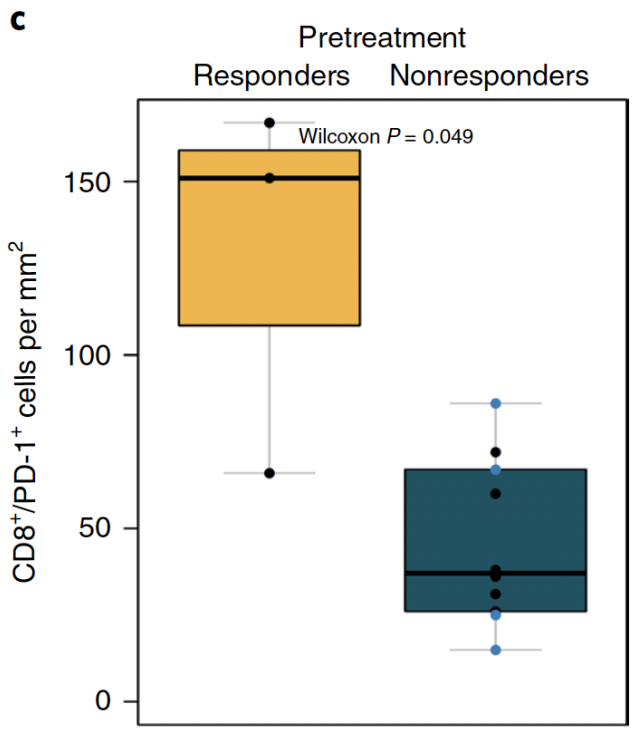
- safety/feasibility

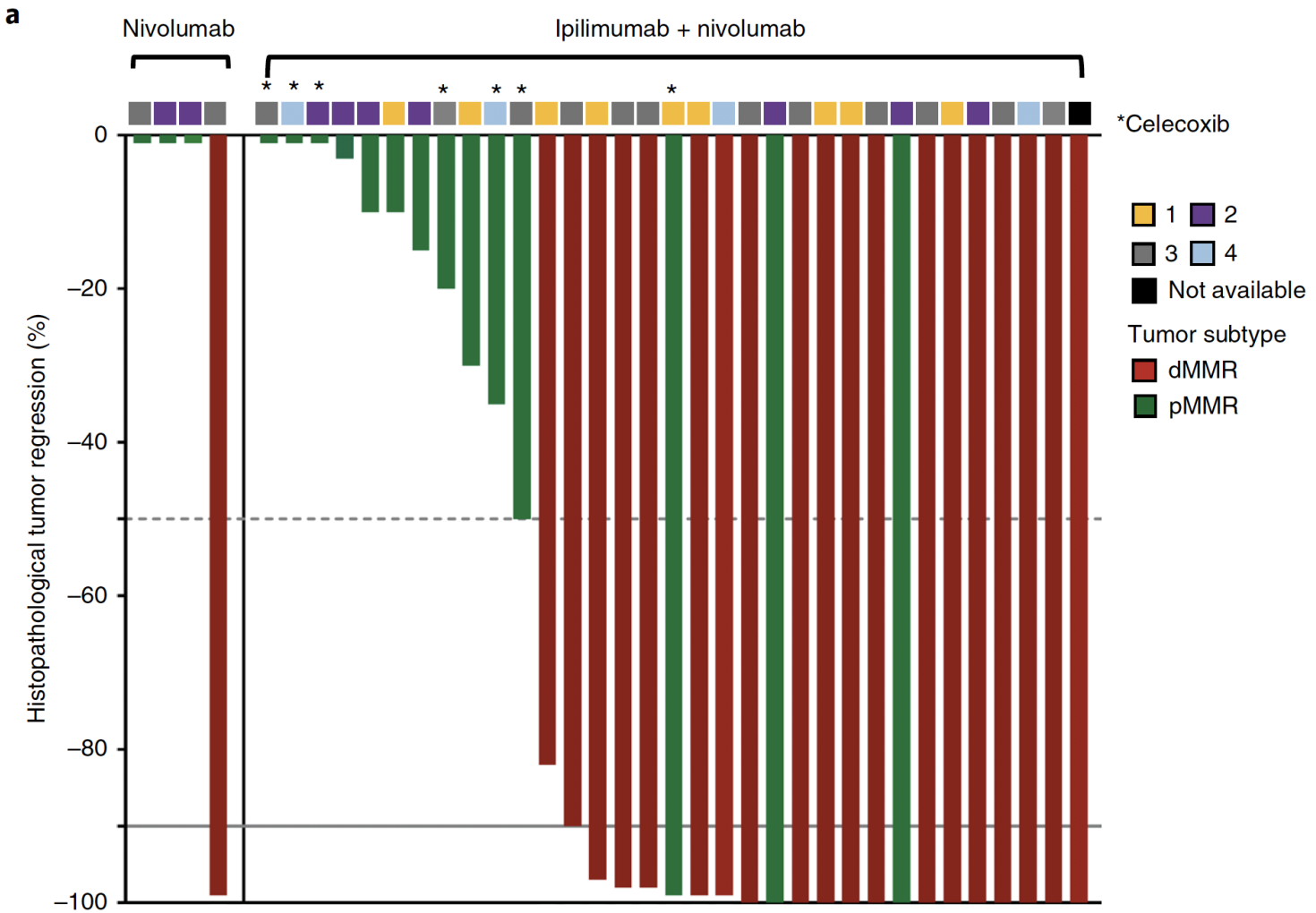
Secondary objectives:

- efficacy
- associations between response and
  - tumor mutational burden (TMB)
  - interferon $(IFN)_\gamma$ gene signatures
  - T-cell infiltration
  - TCR clonality



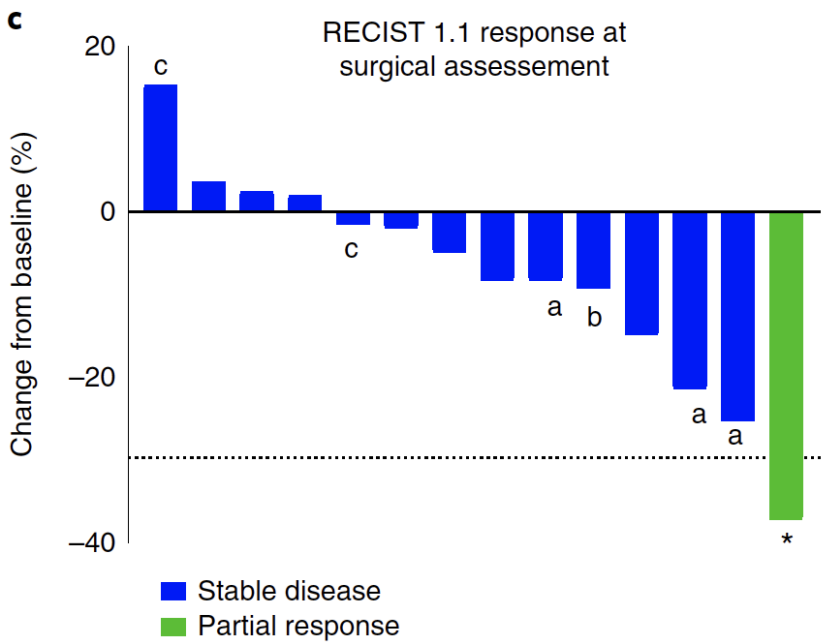
NICHE: Response Rate

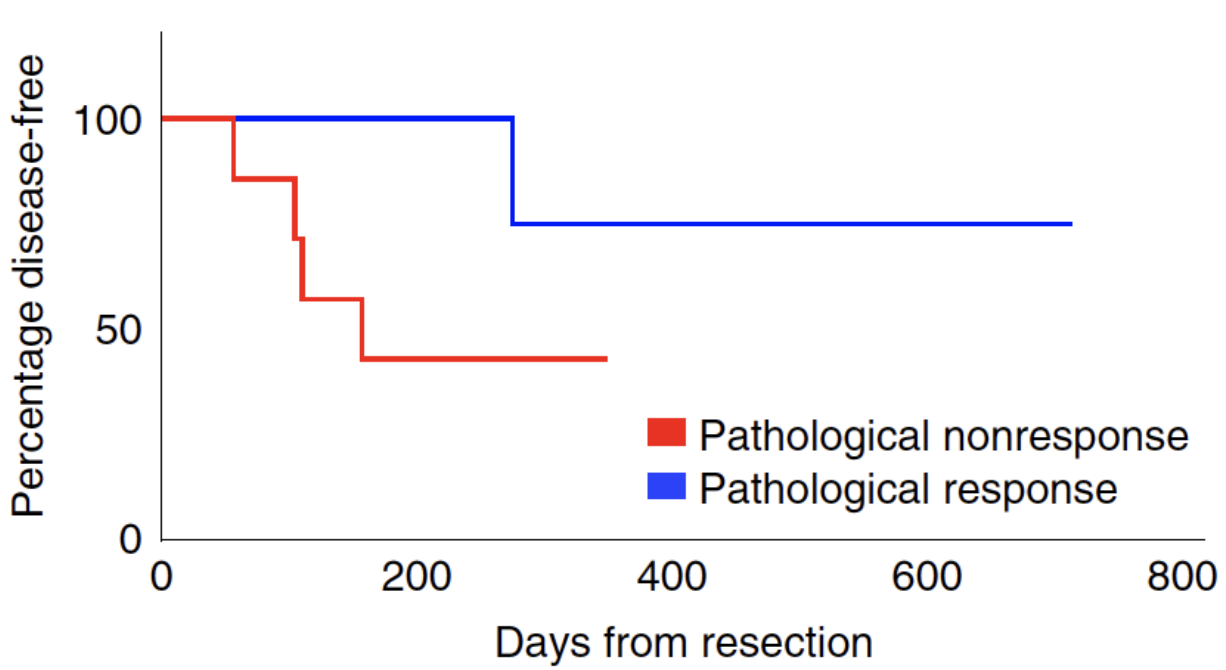




nature cancer
ARTICLES
https://doi.org/10.1038/s43018-021-00234-4
Check for updates

Neoadjuvant cabozantinib and nivolumab convert locally advanced hepatocellular carcinoma into resectable disease with enhanced antitumor immunity





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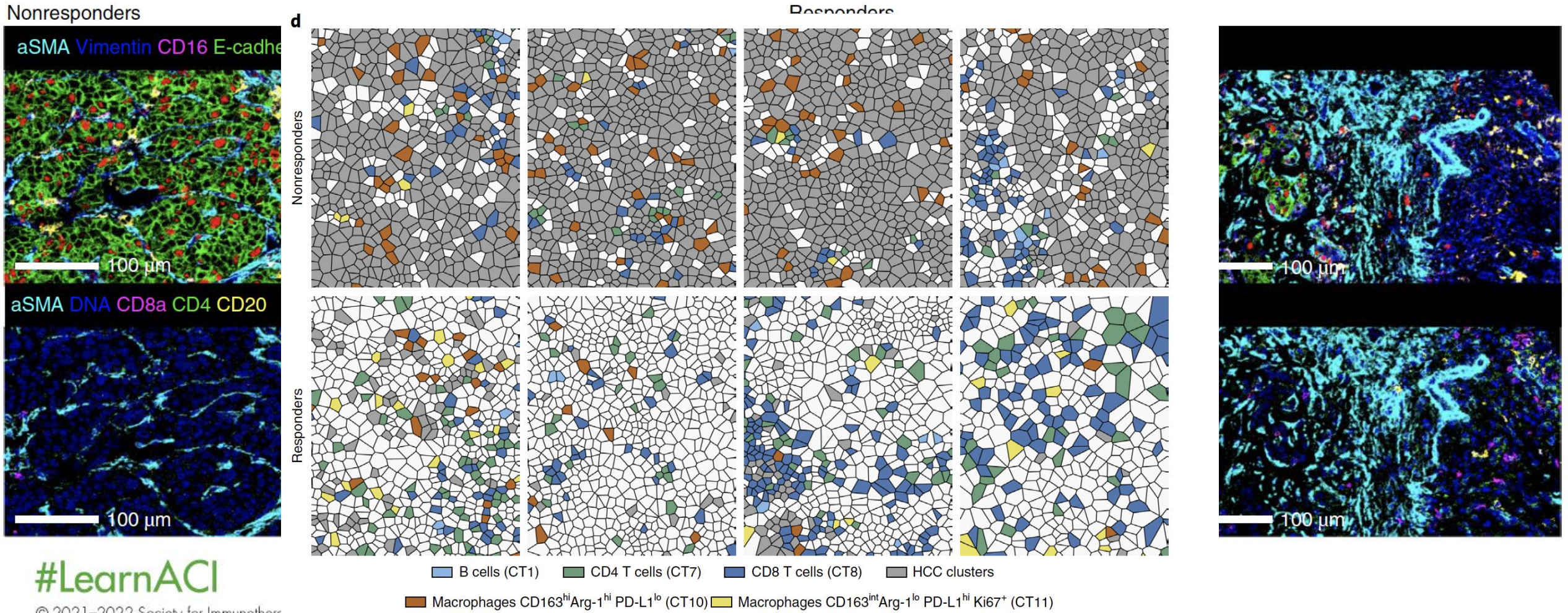
Proximity between lymphoid and macrophage subtypes is key determinant of response to cabozantinib and nivolumab



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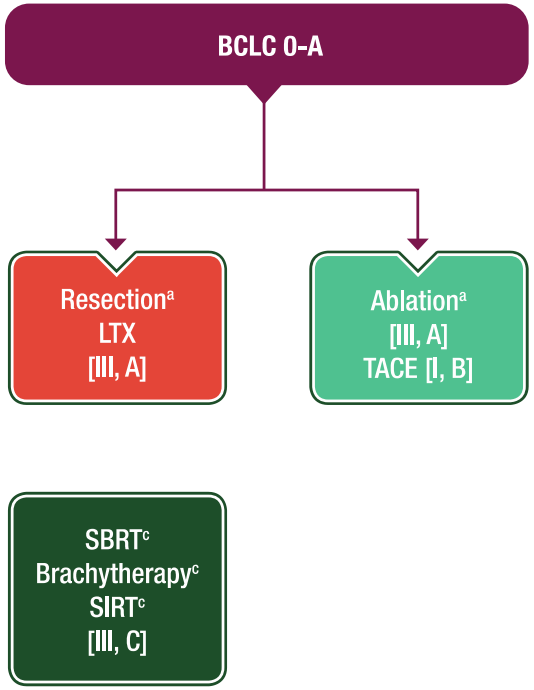
IO-combinations in early stage



Adjuvant

Monotherapy

KEYNOTE-937 (HCC)
Pembrolizumab vs placebo

Adjuvant

Combination

EMERALD-2 (HCC)
Durvalumab ± Bevacizumab vs placebo

Adjuvant

Monotherapy

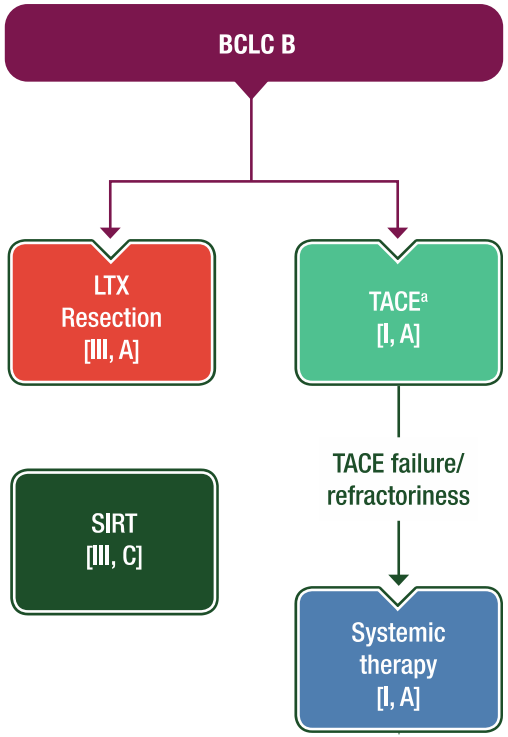
CHECKMATE-9DX (HCC)
Nivolumab vs placebo

Adjuvant

Combination

Imbrave-050
Atezolizizumab ± Bevacizumab vs placebo

IO-combinations in intermediate stage



- **TACE-3**:

  TACE ± Nivolumab
- **ML42612:**

  TACE ± Atezolizumab + Bevacizumab
- **EMERALD-1:**

  TACE ± Durvalumab + Bevacizumab
- **LEAP-012:**

  TACE ± Pembrolizumab + Lenvatinib
- ~~**CHECKMATE 74 W**~~

  ~~TACE ± Nivo/ IPI vs Nivo~~

Stopped due to slow recruitment

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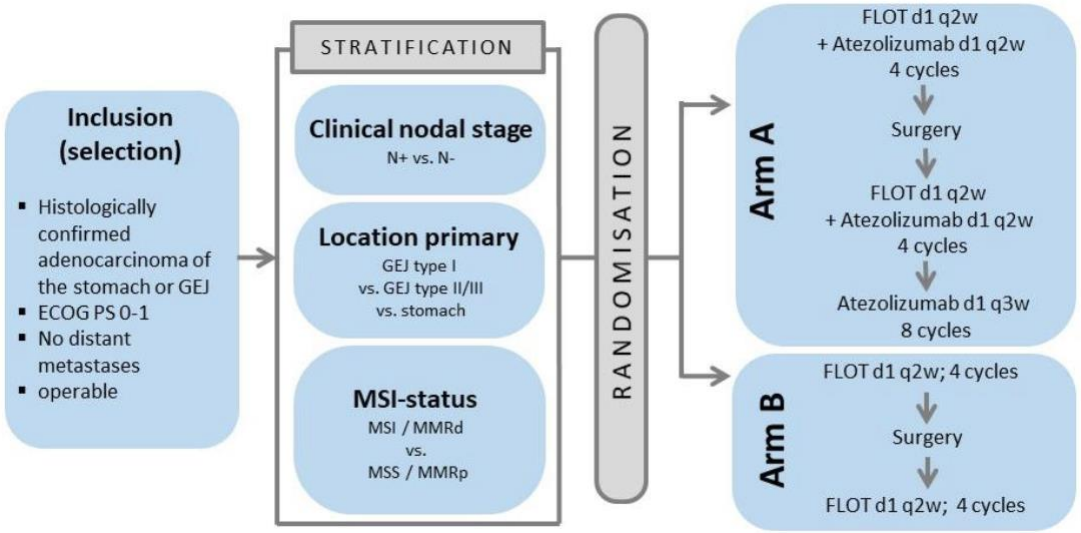
Pathological regression in patients with microsatellite instability (MSI) receiving perioperative atezolizumab in combination with FLOT vs. FLOT alone for resectable esophagogastric adenocarcinoma: Results from the DANTE trial of the German Gastric Group at the AIO and SAKK.

Salah-Eddin Al-Batran[1,2], Sylvie Lorenzen[3], Nils Homann[4], Peter C. Thuss-Patience[5], Michael Schenk[6], Udo Lindig[7], Albrecht Kretzschmar[8], Vera Heuer[9], Eray Goekkurt[10], Georg Martin Haag[11], Jorge Riera Knorrenschild[12], Claus Bolling[13], Ralf Hofheinz[14], Alexander Rheinhard Siebenhuener[15], Natsumi Irahara[16], Christina Kopp[1], Lisa Waberer[1], Claudia Pauligk[1], Thorsten O. Goetze[1,2], Timo Gaiser[17]



Pathological regression	pMMR (MSS) N=222		dMMR (MSI) N=23	
Complete (pCR/TRG1a)	47	(21.2%)	11	(47.8%)
Subtotal (pSR/TRG1b)	41	(18.5%)	4	(17.4%)
Partial (pPR/TRG2)	58	(26.1%)	3	(13.0%)
Minor or no regression	51	(23.0%)	5	(21.7%)
Not evaluable	25	(11.3%)	0	

	dMMR (MSI) N=23			
Pathological regression	FLOT N=13		Atezolizumab/FLOT N=10	
Complete (pCR/TRG1a)	5	(38.5%)	6	(60.0%)
Subtotal (pSR/TRG1b)	2	(15.4%)	2	(20.0%)
Partial (pPR/TRG2)	1	(7.7%)	2	(20.0%)
Minor or no regression	5	(38.5%)	0	

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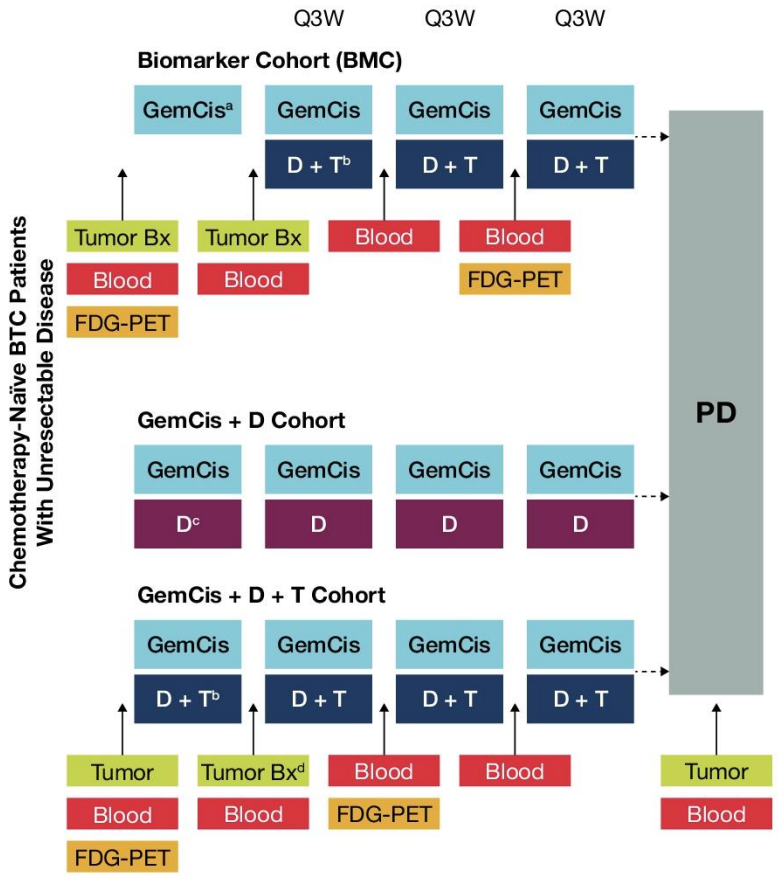
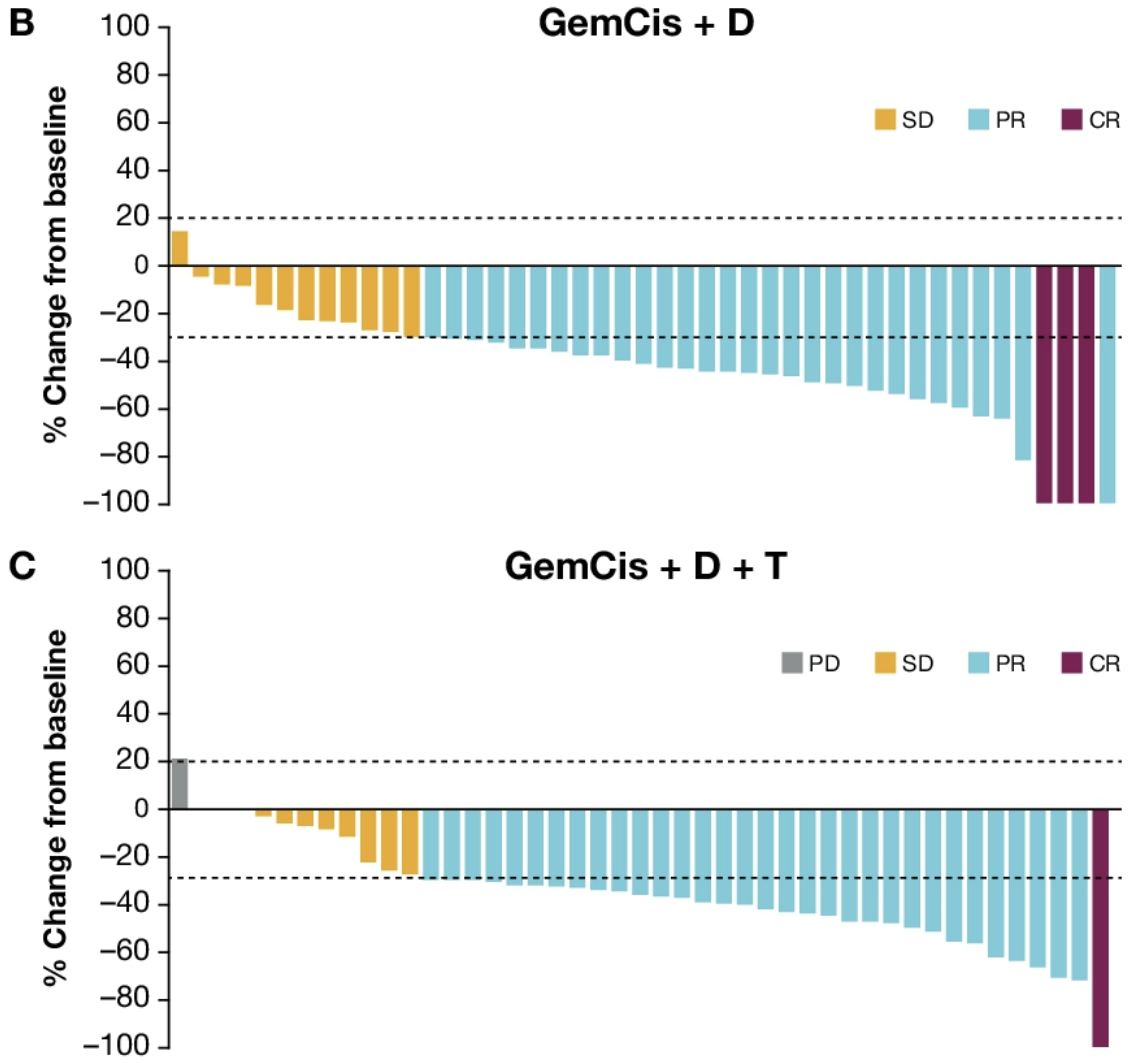
Immunotherapy in BTC: BTC-1st MEDITREME





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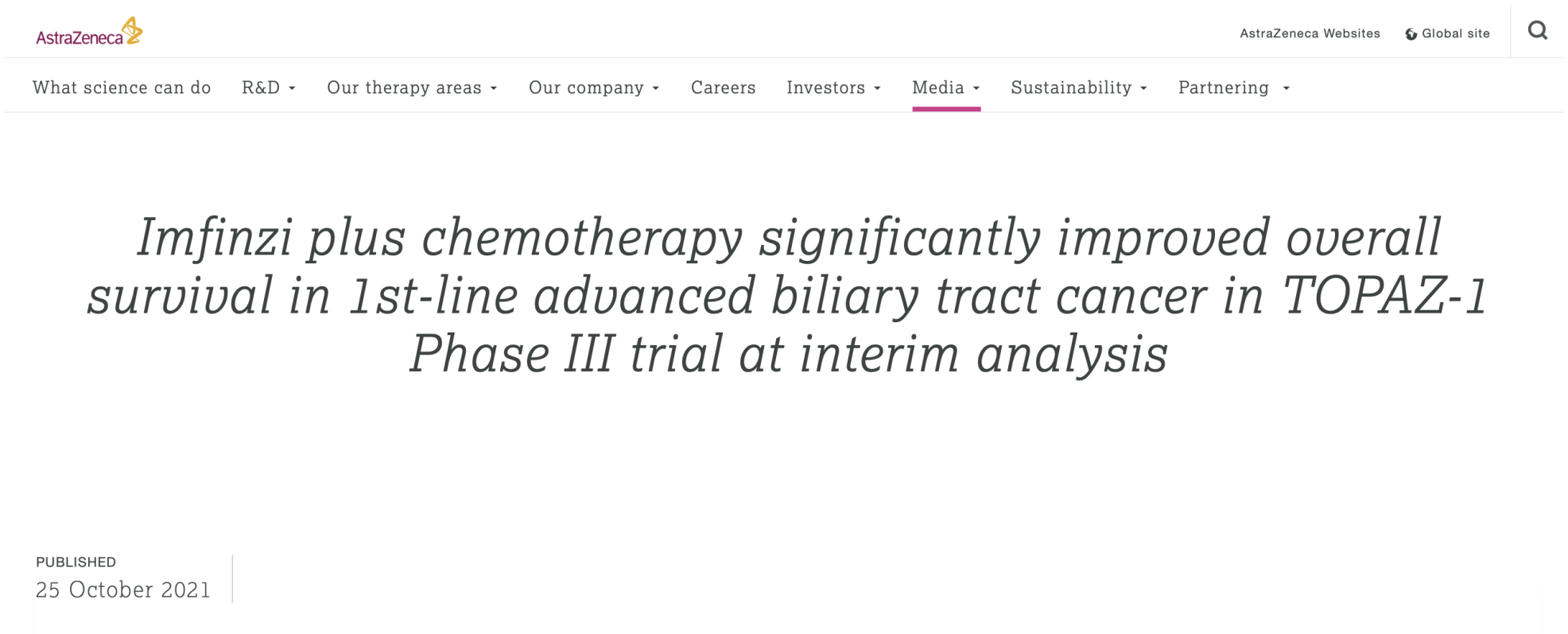
Oh D-Y | Abstract 4520 | ASCO 2020

Ongoing phase 3 studies (first-line setting)



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ESMO World Congress on Gastrointestinal Cancer

Pembrolizumab Plus Trastuzumab and Chemotherapy for HER2+ Metastatic Gastric or Gastroesophageal Junction Cancer: Initial Findings of the Global Phase 3 KEYNOTE-811 Study

Yelena Y. Janjigian,[1] Akihito Kawazoe,[2] Patricio Yañez,[3] Suxia Luo,[4] Sara Lonardi,[5] Oleksii Kolesnik,[6] Olga Barajas,[7] Yuxian Bai,[8] Lin Shen,[9] Yong Tang,[10] Lucjan S. Wyrwicz,[11] Kohei Shitara,[2] Shukui Qin,[12] Eric Van Cutsem,[13] Josep Tabernero,[14] Lie Li,[15] Chie-Schin Shih,[15] Pooja Bhagia,[15] Hyun Cheol Chung,[16] on behalf of the KEYNOTE-811 Investigators

Key Eligibility Criteria
- Unresectable or metastatic gastric or GEJ adenocarcinoma
- No prior systemic therapy in advanced setting
- HER2-positive tumor by central review (IHC 3+ or IHC 2+ ISH+)
- ECOG PS 0 or 1

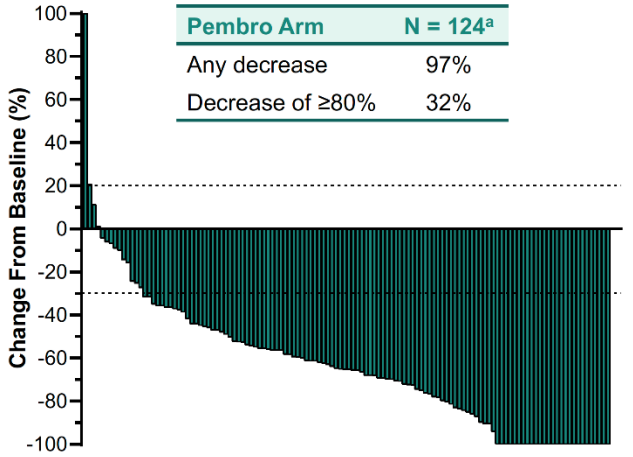
Stratification Factors
- Geographic region (Australia/Europe/Israel/North America vs Asia vs ROW)
- PD-L1 CPS (≥1 vs <1)
- Chemotherapy choice (FP vs CAPOX)

R 1:1
N ≈ 692

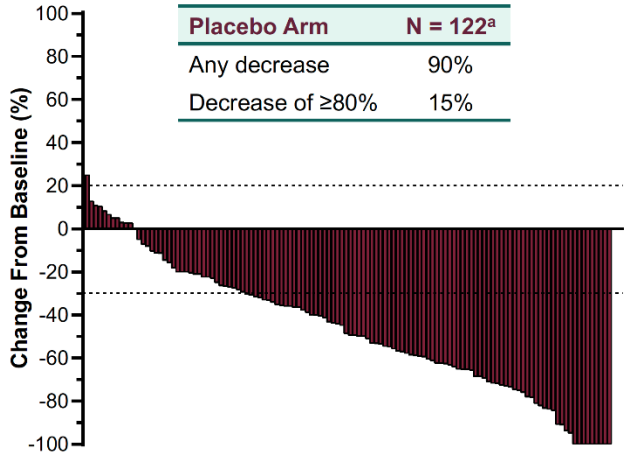
Pembrolizumab 200 mg IV Q3W + Trastuzumab and FP or CAPOX[a] for up to 35 cycles

Placebo IV Q3W + Trastuzumab and FP or CAPOX[a] for up to 35 cycles

End Points
- **Dual primary:** OS and PFS per RECIST v1.1 by BICR
- **Key secondary:** ORR and DOR per RECIST v1.1 by BICR and safety



Pembro Arm	N = 124[a]
Any decrease	97%
Decrease of ≥80%	32%



Placebo Arm	N = 122[a]
Any decrease	90%
Decrease of ≥80%	15%

ORR and DCR, % (95% CI)	Pembro Arm (N = 133)	Placebo Arm (N = 131)
ORR	**74.4% (66.2-81.6)**	**51.9% (43.0-60.7)**
ORR difference[a]	**22.7% (11.2-33.7) *P* = 0.00006**	
DCR	96.2% (91.4-98.8)	89.3% (82.7-94.0)

Best Response, n (%)	Pembro Arm (N = 133)	Placebo Arm (N = 131)
CR	**15 (11%)**	**4 (3%)**
PR	**84 (63%)**	**64 (49%)**
SD	29 (22%)	49 (37%)
PD	5 (4%)	7 (5%)
Not evaluable	0	2 (2%)
Not assessed	0	5 (4%)

DOR[b]	Pembro Arm (N = 99)	Placebo Arm (N = 68)
Median (range)	10.6 mo (1.1+ to 16.5+)	9.5 mo (1.4+ to 15.4+)
≥6-mo duration	70%	61%
≥9-mo duration	58%	51%

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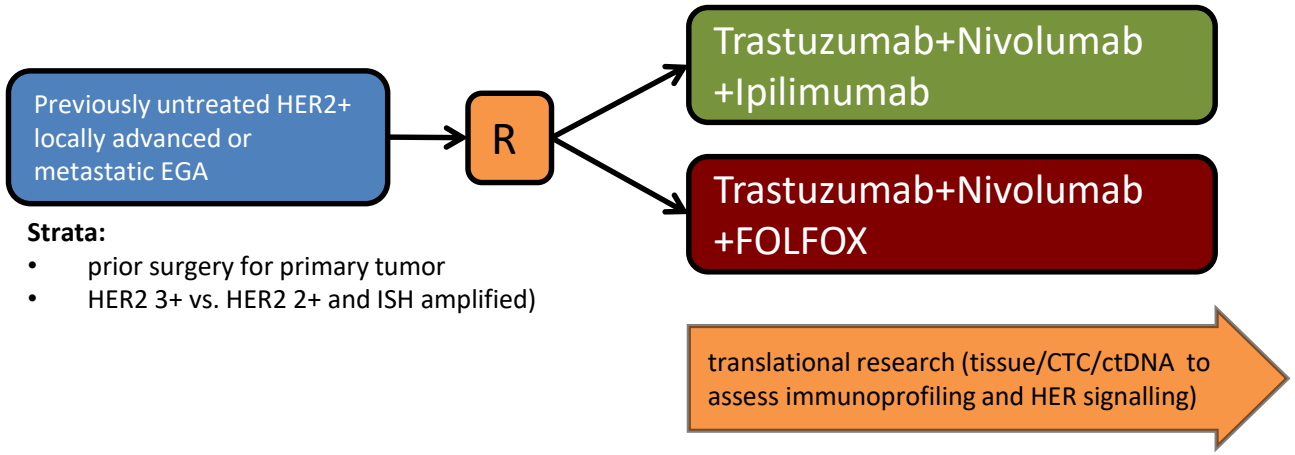
2021 ESMO congress

Ipilimumab or FOLFOX in combination with Nivolumab and Trastuzumab in previously untreated HER2 positive Esophago Gastric Adenocarcinoma – the randomized AIO INTEGA trial.

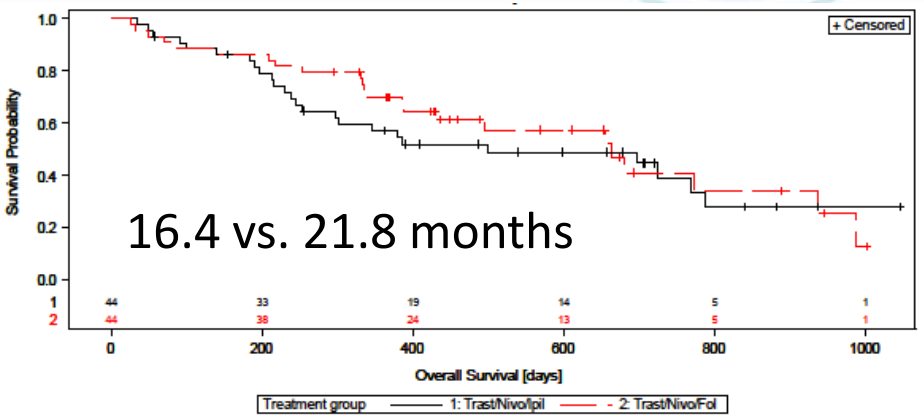
Alexander Stein



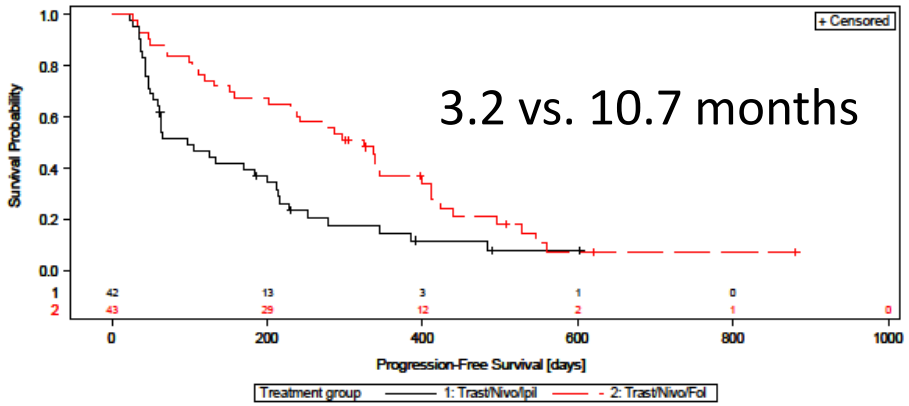
Strata:

- prior surgery for primary tumor
- HER2 3+ vs. HER2 2+ and ISH amplified)

Overall survival



Progression free survival



-- Trast/Nivo/Ipi -- Trast/Nivo/FOLFOX

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2021 ESMO congress

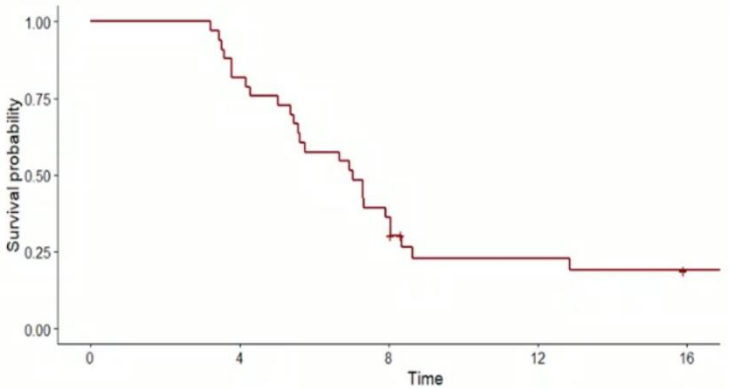
Temozolomide (TMZ) priming followed by combination with low-dose ipilimumab and nivolumab in patients with microsatellite stable (MSS), MGMT silenced metastatic colorectal cancer (mCRC): The MAYA study

***Pietrantonio F.**, Morano F., Lonardi S., Raimondi A., Salvatore L., Marmorino F., Murgioni S., Pella N., Antonuzzo L., Ritorto G., Zaniboni A., Ratti M., Palermo F., Pagani F., Prisciandaro M., Cagnazzo C., Capone I., Milione M., Di Bartolomeo M., de Braud F.*

Overall, **12/33** patients who started the Second Treatment Phase had a PFS > 8 months

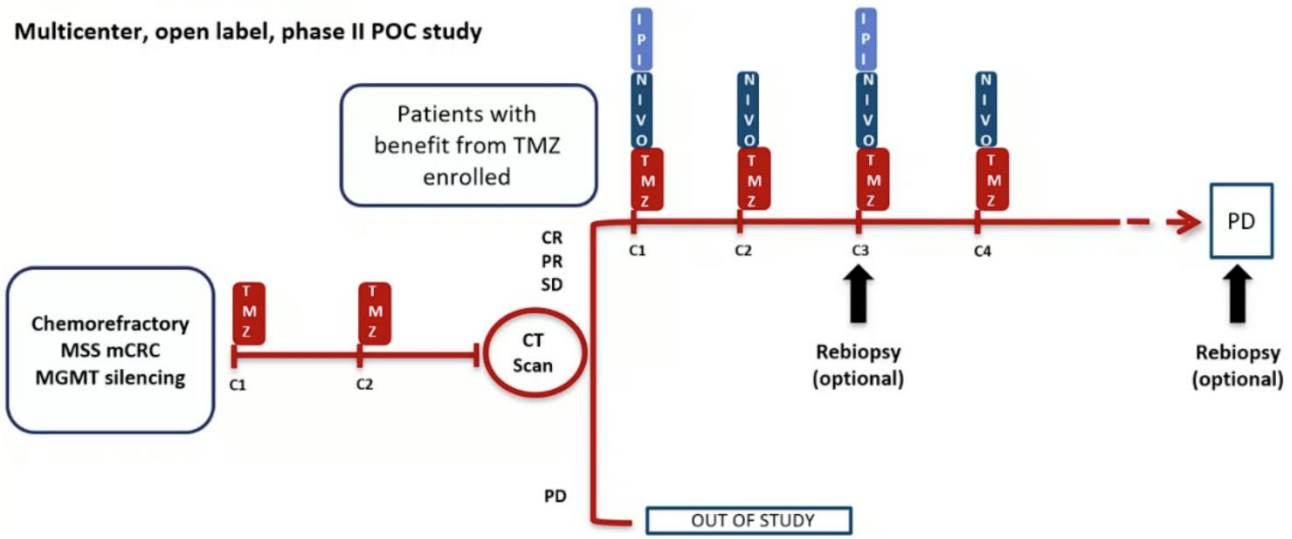
The primary endpoint of MAYA was met: 8 month PFS rate 36%

Median PFS: 7.1 months [95% CI, 5.6-8.4]

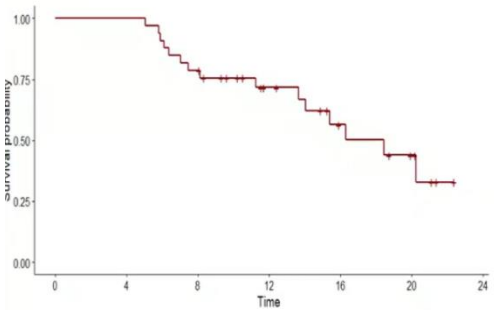


At the data cut-off date of 5th Aug 2021, median follow up was 16.0 mos

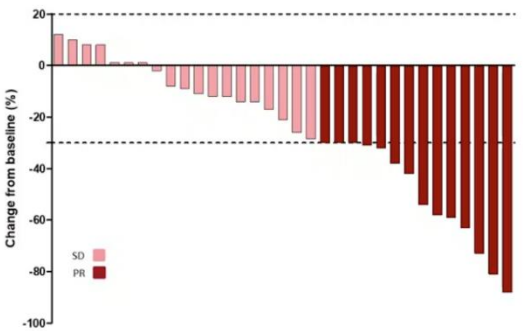
Multicenter, open label, phase II POC study



Median OS: 18.4 months [95% CI, 14-NA]



The **ORR** to the whole strategy was **42%** (14/33)



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Claudin 18.2 directed CAR-T-cells

A multicenter, open-label, phase I ongoing study.

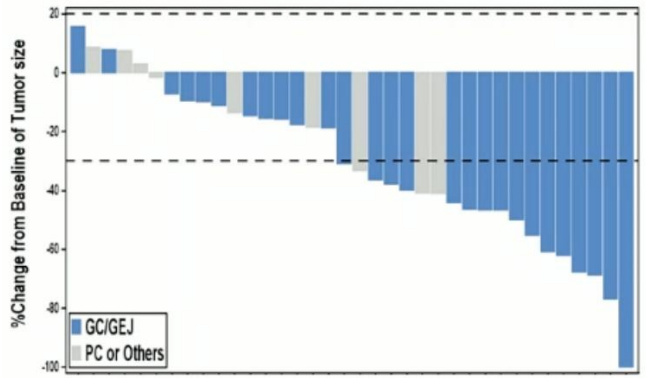
- 18-75 years
- Previously treated advanced digestive system cancers confirmed by pathology
- **CLDN18.2 expression: ≥+,≥10%**
- ECOG:0 or 1

Apheresis → Manufacturing CT041 (2w-3w) → CT041 infusion → Progressive disease or Intolerable toxicity → Survival follow up

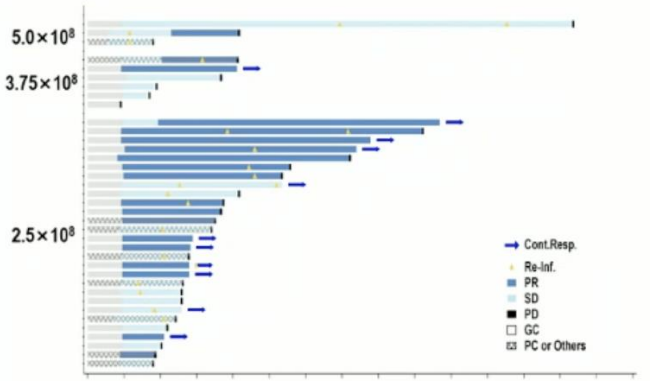
Apheresis → Bridging chemotherapy → Preconditioning therapy[#] → CT041 infusion

Reinfusion (Depend on Subject's condition)

Thirty-six of the 37 subjects had target lesions. 31 subjects had different degrees of shrinkage of target lesions. According to RECIST 1.1, ORR and DCR reached **48.6%** (18/37) and **73.0%** (27/37) respectively.



GC/GEJ: gastric carcinoma / gastroesophageal junction
PC: pancreatic adenocarcinoma



Qin et al. @ESMO 2021

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vogela@me.com

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