



Review of the year 2020

Metastasiertes Mammakarzinom

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Diakovere Henriettenstift Hannover

Conflicts of Interest

- **Berater/Ad-Boardtätigkeiten/Referententätigkeiten**
- **Roche**
- **Novartis**
- **Genomic Health**
- **Lilly**
- **Pfizer**
- **AstraZeneca**
- **MSD**
- **Esai**

Studiendesign

N=156

R

Everolimus 10 mg

Woche 1-3: 4X2,5mg Tag (verblinded)

Woche 4-24: 10mg/Tag (open-label entsprechend Fachinformation)

vorgeschaltete Dosiseskulation von Everolimus-Plazebo

Woche 1 1x2,5mg Verum + 3x Plazebo/Tag;

Woche 2: 2x 2,5mg Verum +2x Plazebo/Tag;

Woche 3: 3x 2,5 mg Verum + 1x Plazebo/Tag;

Woche 4-24: 10mg/Tag (open-label entsprechend Fachinformation)

➔ Patientenprofil entsprechend Indikation für Everolimus
+ Exemestan in beiden Armen

Follow-up: EOT Visite (Woche 25-28)

Statistische Annahme:

Control arm: 40% Mukositis

Escalation arm: 20% Mukositis

Zeitplan Desiree

- Studienstart Jun 2015
- First patient in Jun 2015
- Last patient in QIV 2020
- Anzahl der Zentren 29



Geschafft ! HERZLICHEN DANK AN ALLE Zentren und Referenten

- Last Patient Out Mai 2021
- Patientenzahl 156
- Finale Analyse Mai/Juni 2021
- Studienergebnisse ESMO oder SABCS 21



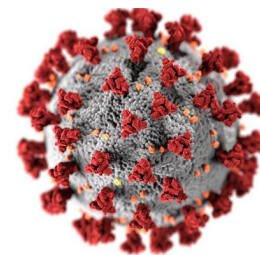
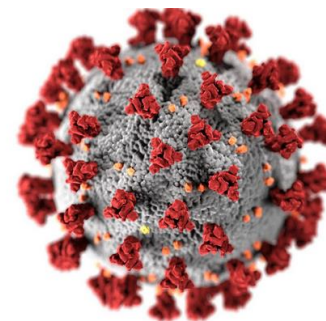
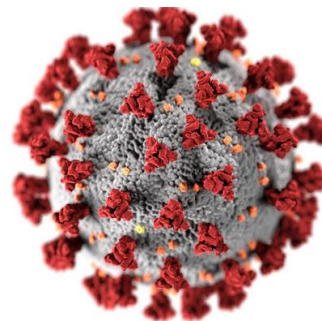
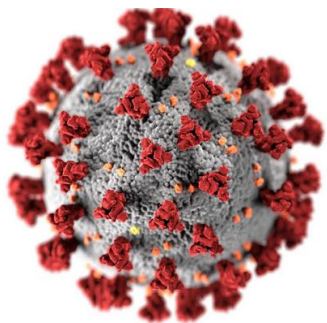
GBG Jahrestreffen 2020

- Das letzte Treffen mit Anwesenheit GBG 2020



Metastasiertes Mammakarzinom

Review of the year 2020





Metastasiertes Mammakarzinom Review of the year 2020

■ Her2 positives met. Mammakarzinom

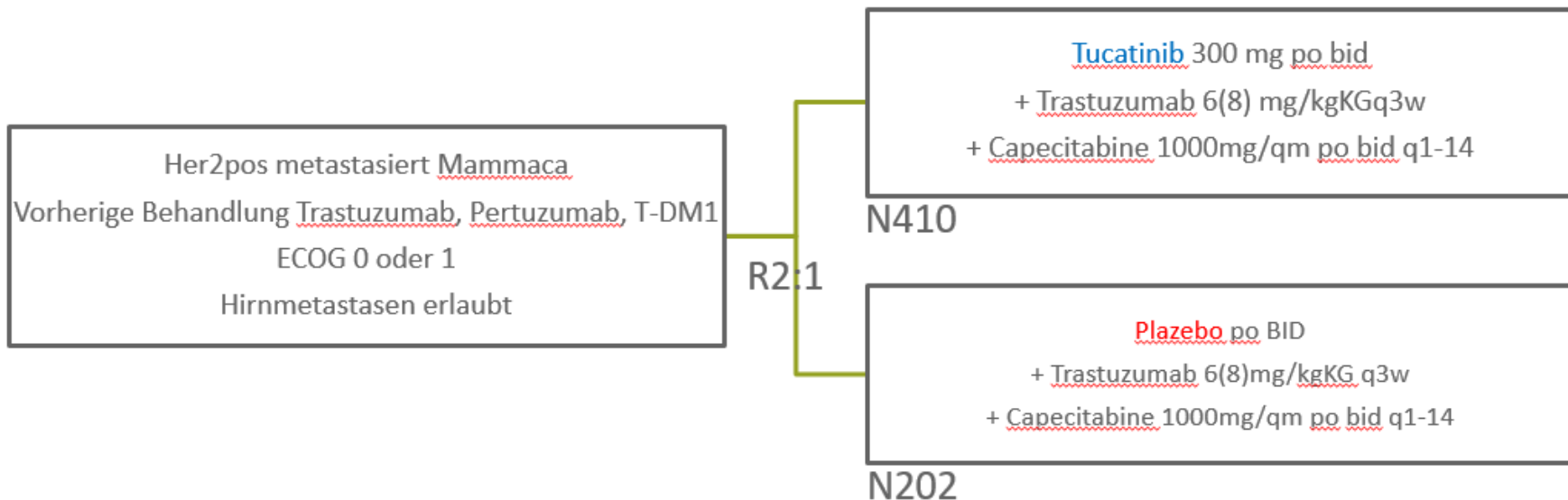
1) Her 2 Climb

2) Destiny 01

3) Pertain

Her2 positives met. Mammakarzinom

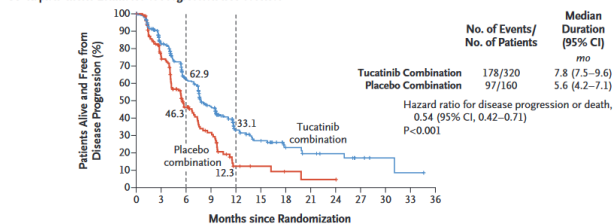
Her2 Climb- Studiendesign



Her2 Climb

PFS Gesamtgruppe nach Rando von 480

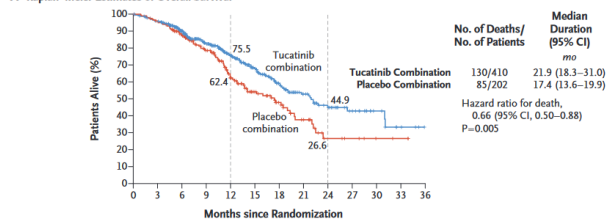
A Kaplan-Meier Estimates of Progression-free Survival



No. at Risk	0	3	6	9	12	15	18	21	24	27	30	33	36
Tucatinib combination	320	235	152	98	40	29	15	10	8	4	2	1	0
Placebo combination	160	94	45	27	6	4	2	1	1	0	0	0	0

OS Gesamtgruppe

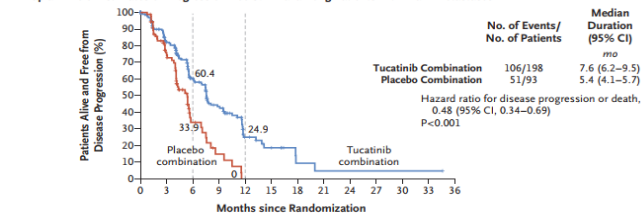
A Kaplan-Meier Estimates of Overall Survival



No. at Risk	0	3	6	9	12	15	18	21	24	27	30	33	36
Tucatinib combination	410	388	322	245	178	123	80	51	34	20	10	4	0
Placebo combination	202	191	160	119	77	48	32	19	7	5	2	1	0

PFS Pat mit Hirnmets

A Kaplan-Meier Estimates of Progression-free Survival among Patients with Brain Metastases

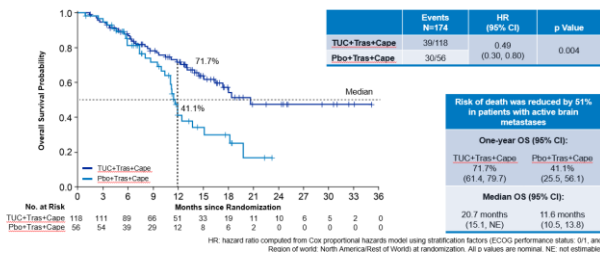


No. at Risk	0	3	6	9	12	15	18	21	24	27	30	33	36
Tucatinib combination	198	144	78	45	14	8	2	1	1	1	1	1	0
Placebo combination	93	49	12	4	0	0	0	0	0	0	0	0	0

Murthy et al NEJM 2020

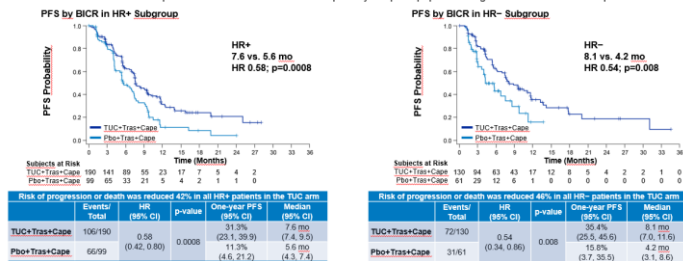
Her2 Climb

OS Benefit in Patients with Active Brain Metastases



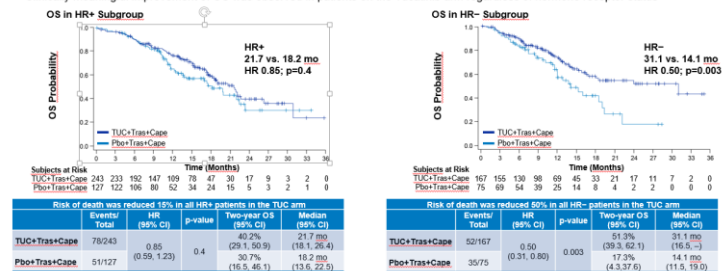
Progression-Free Survival

- PFS benefit was observed in patients in the Tucatinib arm of the primary endpoint population regardless of hormone receptor status



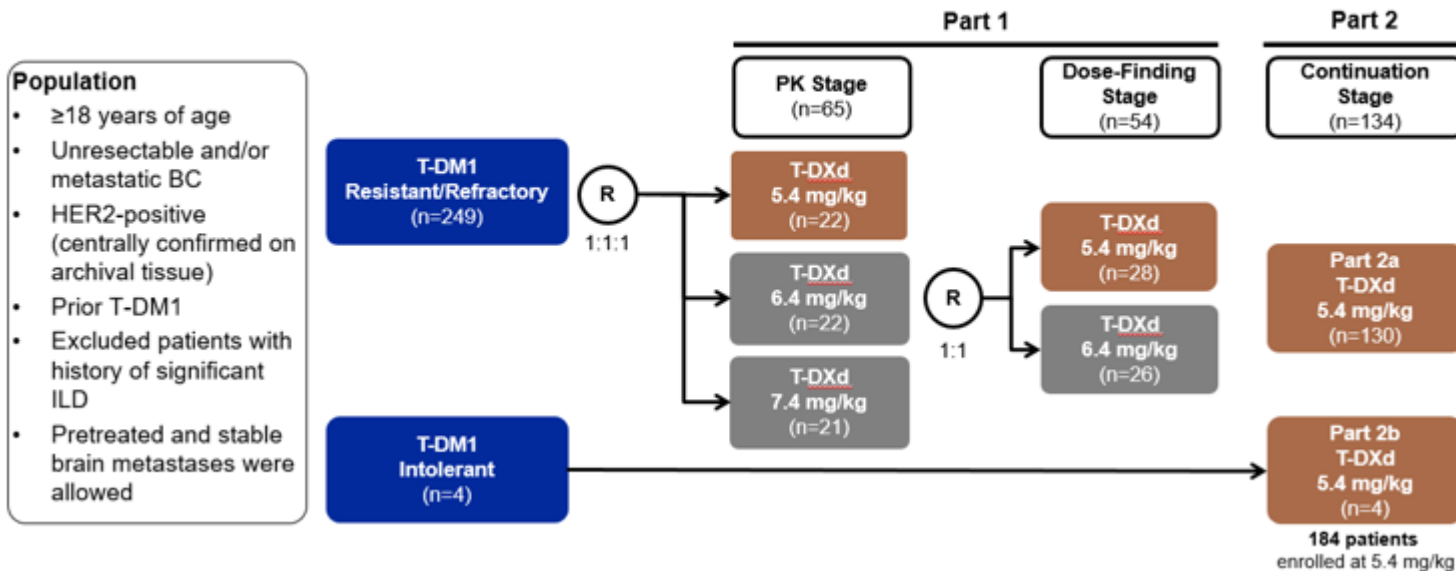
Overall Survival

- Clinically meaningful improvement of OS was observed in patients on the Tucatinib arm regardless of hormone receptor status



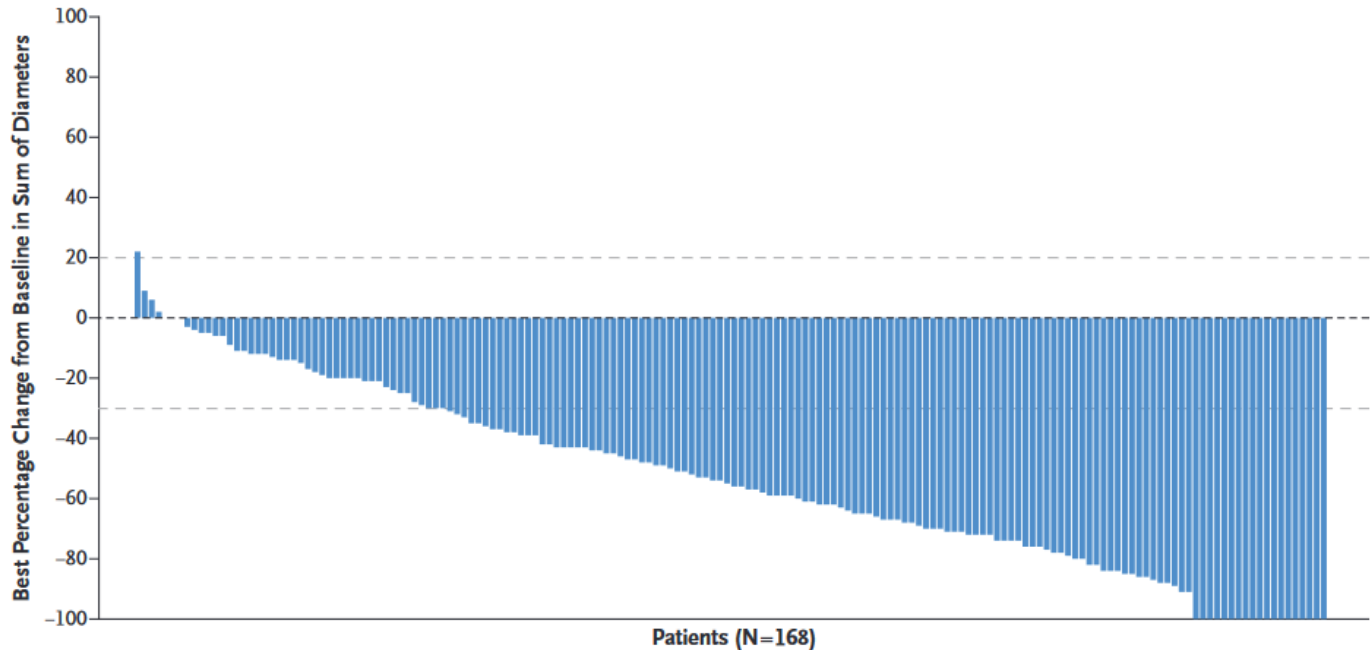
Hamilton E et al. 2020 SABCS Virtual Symposium, Abstract No. PD3-08

Destiny 01-Studiendesign



Destiny 01

A Change from Baseline in Tumor Size



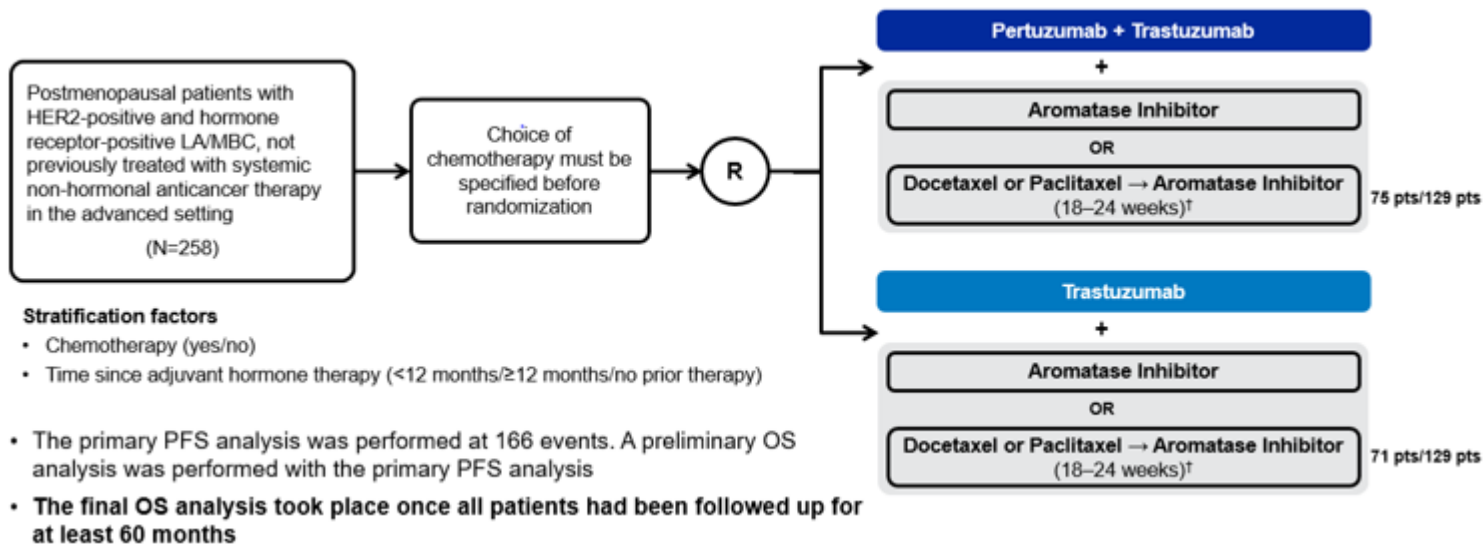
Modi et al NEJM 2020

Destiny 01 Tox: ILD

Interstitial lung disease, n (%)	T-DXd 5.4 mg/kg (N=184)					
	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any grade/ Total
Aug 2019 data cutoff	5 (2.7)	15 (8.2)	1 (0.5)	0	4 (2.2)	25 (13.6)
June 2020 data cutoff	6 (3.3)	16 (8.7)	1 (0.5)	0	5 (2.7)	28 (15.2)

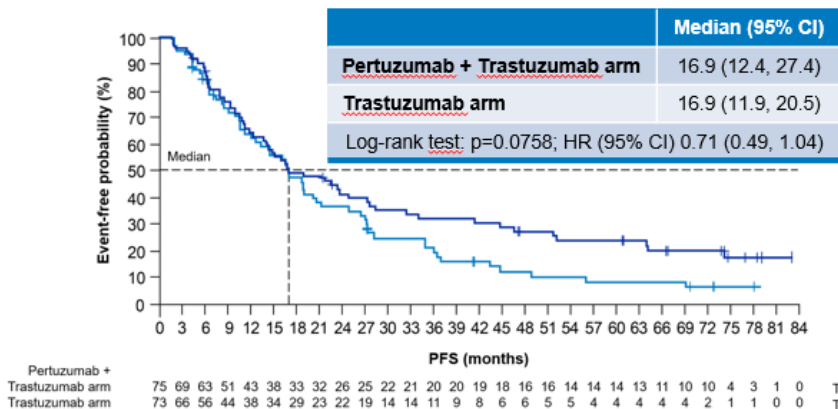
Modi S et al. Spotlight Poster Discussion 3 – Advances in HER2 Positive Disease Abstract No. PD3-06

Pertain Design

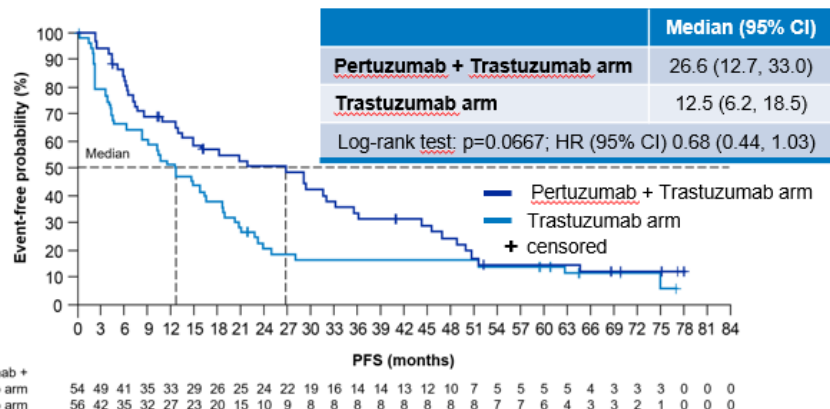


Pertain

Patients who received induction chemotherapy



Patients who did not receive induction chemotherapy



- Overall, PERTAIN provides additional evidence on the role of Pertuzumab + Trastuzumab in the first-line treatment of HER2-positive LA/MBC and suggests that some patients benefit from Pertuzumab + Trastuzumab + AI without induction chemotherapy

Her2 positives met. Mammakarzinom

■ Fazit Her2 -positives met. Mammakarzinom

- 1) Her 2 Climb, Tucatinib PFS Vorteil unabhängig vom HR Status, OS Vorteil deutliche bei den HR negativen, guter Effekt auch für aktive Hirnmets**
- 2) Destiny 01. Trastuzumab –Deruxtecan: Vielversprechend, Phase III ausstehend, Cave Pneumonitis**
- 3) Pertain: Stützt die reine zielgerichtete Therapie, duale Blockade und endokrin. Die Daten zeigen, dass, wollte/müsste man auf eine Induktionschemotherapie verzichten die Hinzunahme von Pertuzumab zur Trastuzumab und endokrinen Therapie erforderlich wird.**



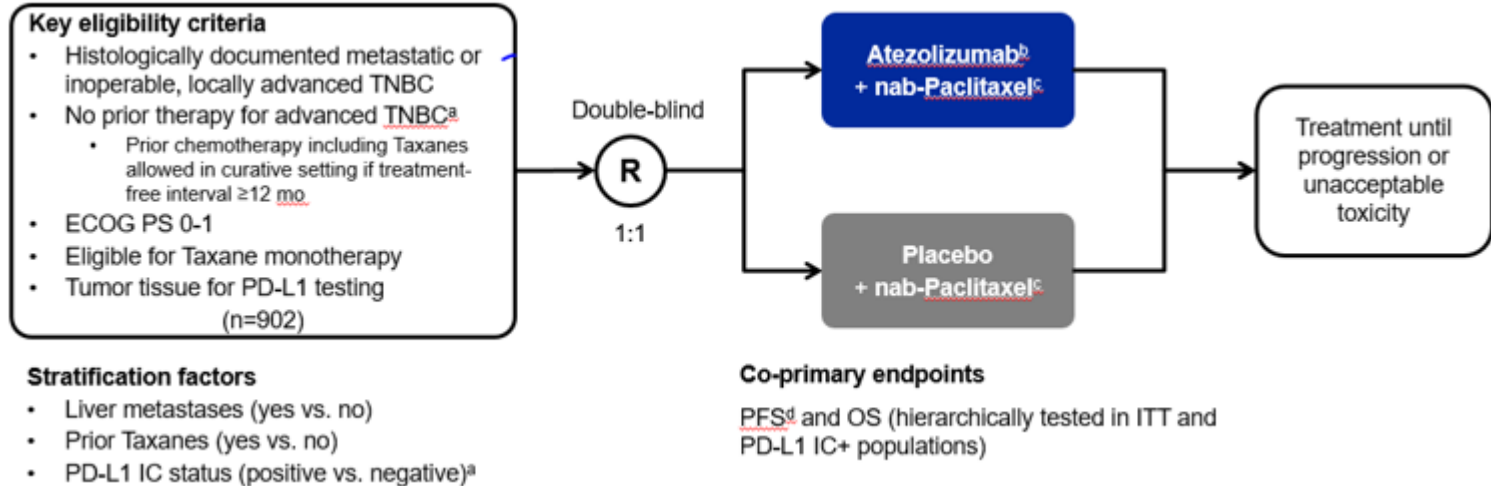
Metastasiertes Mammakarzinom Review of the year 2020

■ Triple negatives met. Mammakarzinom

1) Immunonkologie (Impassion/Keynote)

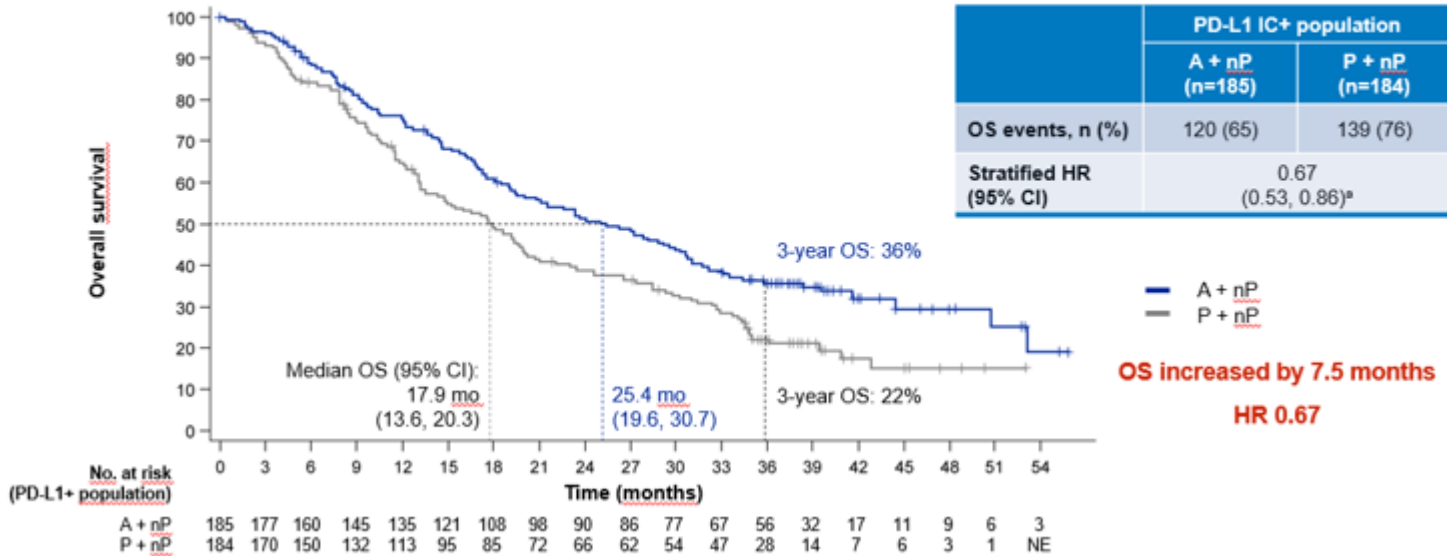
2) Antibody Drug conjugate Sacituzumab –Govitecan (ASCENT)

Impassion 130 Design



Impassion 130 Finale OS Analyse

OS in the PD-L1 IC+ population ←



OS increased by 7.5 months
HR 0.67 ←

Impassion 131 Design

Double-blind Placebo-controlled randomised phase 3 trial

- Metastatic or unresectable locally advanced TNBC
- No prior chemotherapy or targeted therapy for advanced TNBC
- Previous eBC treatment completed ≥ 12 months before randomisation
- Taxane eligible
- Measurable disease
- ECOG PS 0/1

Stratification

- Prior Taxane (yes vs. no)
- Tumour PD-L1 status (IC $< 1\%$ vs. $\geq 1\%$)*
- Liver metastases (yes vs. no)
- Geographical region (N America vs. W Europe/Australia vs. E Europe/Asia Pacific vs. S America)

R

2:1

**Atezolizumab 840 mg d1 & 15 +
Paclitaxel 90 mg/m² d1, 8 & 15**

8–10 mg Dexamethasone or equivalent for at least the first 2 infusions, cycles repeated q28d

**Placebo d1 & 15 +
Paclitaxel 90 mg/m² d1, 8 & 15**

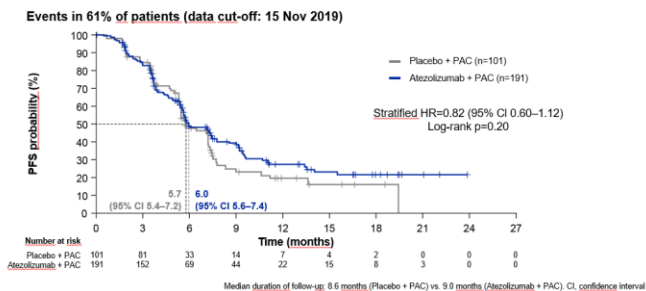
Primary endpoint: PFS (investigator assessed)

Secondary endpoints include:

- OS, ORR, PFS (IRC assessed)
- PROs
- Safety
- Translational research

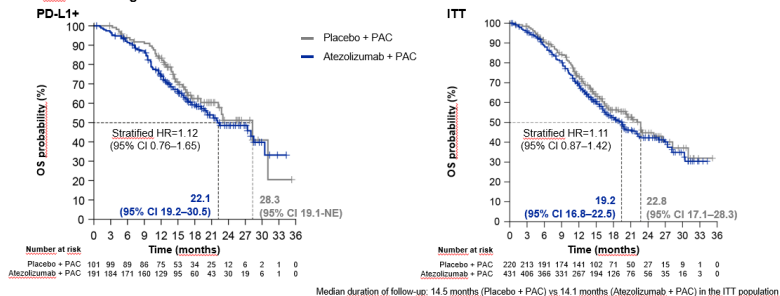
Impassion 131 Results

Primary Analysis: PFS in the PD-L1+ population

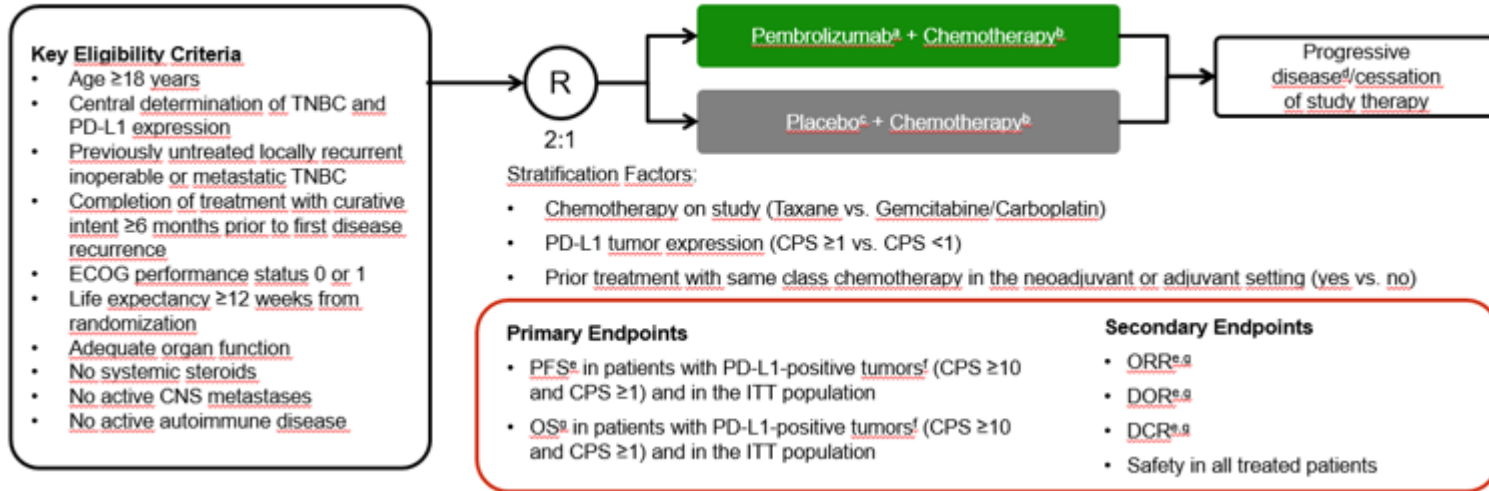


Updated OS

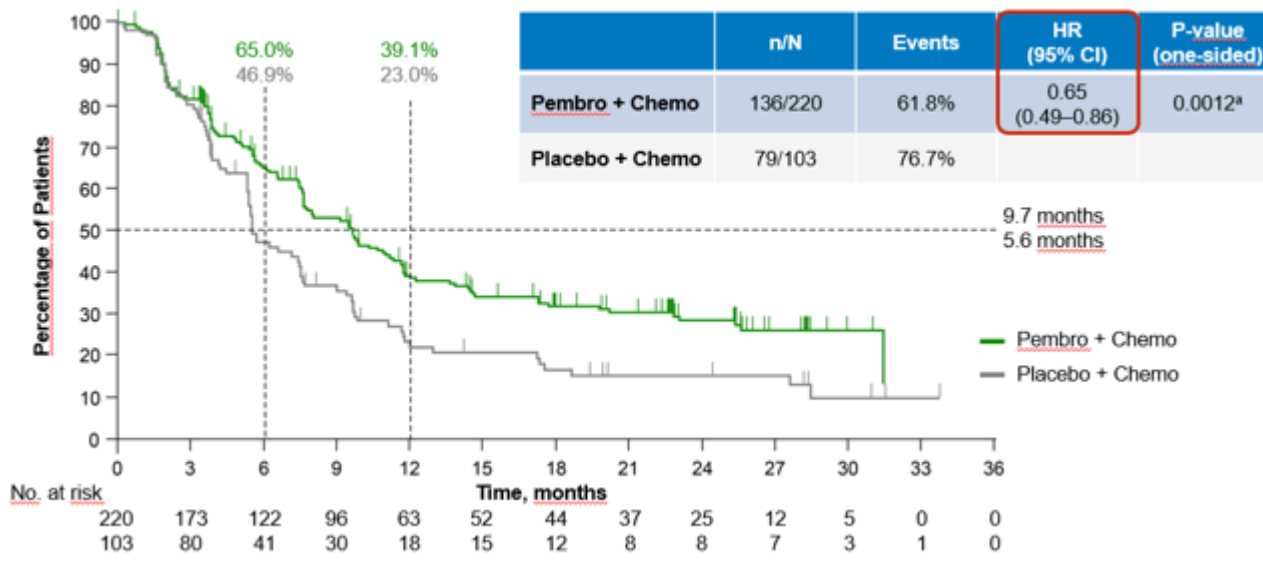
Data cut-off 19 Aug 2020



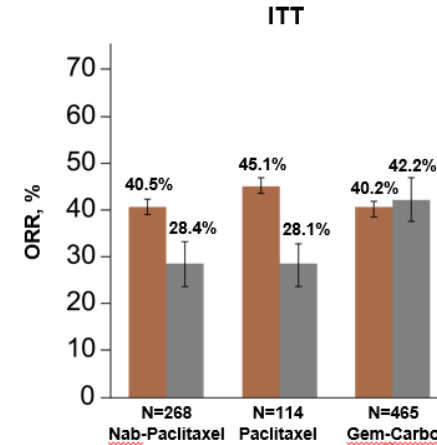
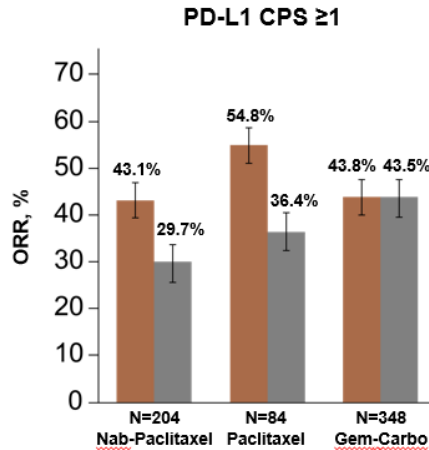
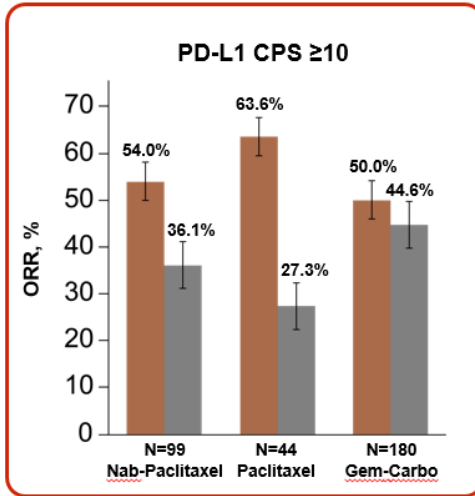
Keynote 355 Design



Keynote 355 PFS PDL1 CPS>10



Keynote 355 ORR /CPS und CTX



■ Pembro + Chemo

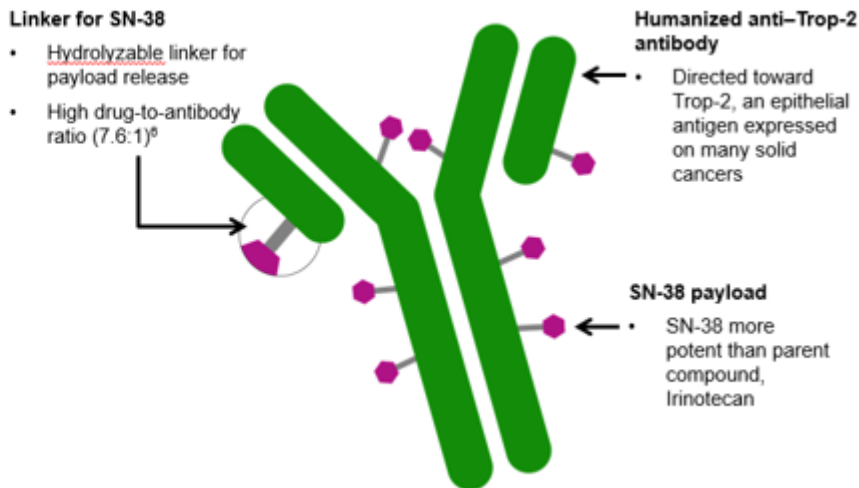
■ Placebo + Chemo

Immunonkologie

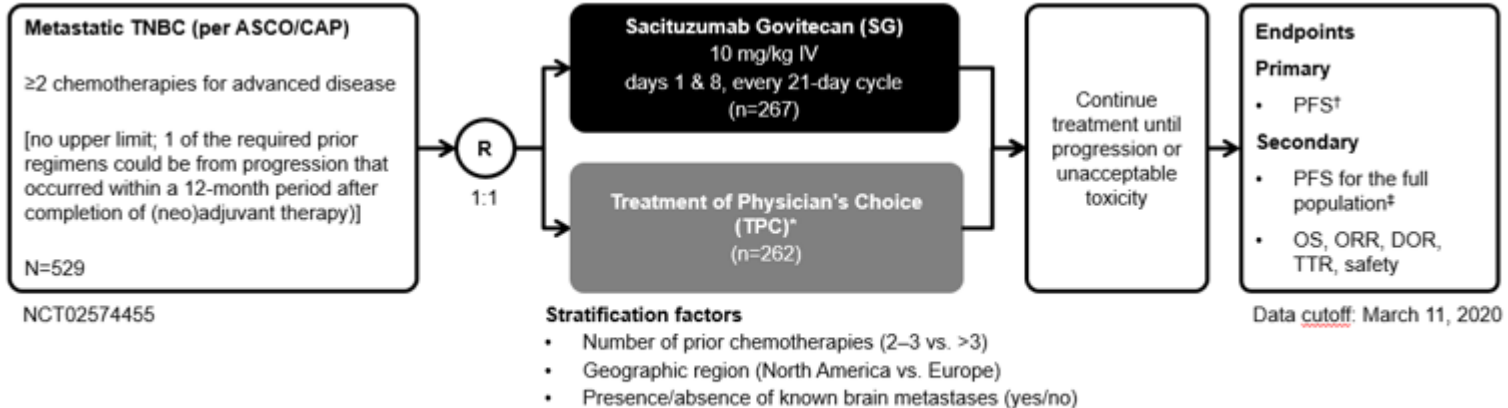
1L Metastatic	<u>IMpassion</u> 130 ³	Nab-Paclitaxel ± Atezolizumab	PFS: HR 0.80, p=0.0021	≥1% cutoff**	Atezo: 50.8% Control: 59.7%	OS ✓ ✓ PFS: HR 0.63, p<0.001 {PD-L1 IC+}
	KEYNOTE- 355 ⁴	Pembrolizumab vs. Nab-Paclitaxel/Paclitaxel/Carboplatin + Gemcitabine	PFS: HR 0.82 (0.69–0.97)	CPS ≥1 or CPS ≥10*	<u>Pembro/Control</u> CPS ≥1: 75.1%/75.1% CPS ≥10: 38.9%/36.7%	✓ PFS: HR 0.65, p 0.0012 (CPS ≥10)

ASCENT ADC

- Trop-2 is expressed in all subtypes of breast cancer and linked to poor prognosis^{1,2}
- SG is distinct from other ADCs³⁻⁶
 - Antibody highly specific for Trop-2
 - High drug-to-antibody ratio (7.6:1)
 - Internalization and enzymatic cleavage by tumor cell not required for the liberation of SN-38 from the antibody
 - Hydrolysis of the linker also releases the SN-38 cytotoxic extracellularly in the tumor microenvironment, providing a bystander effect
- Granted accelerated approval by the FDA for metastatic TNBC and fast-track designation in metastatic urothelial cancer⁷



ASCENT Design

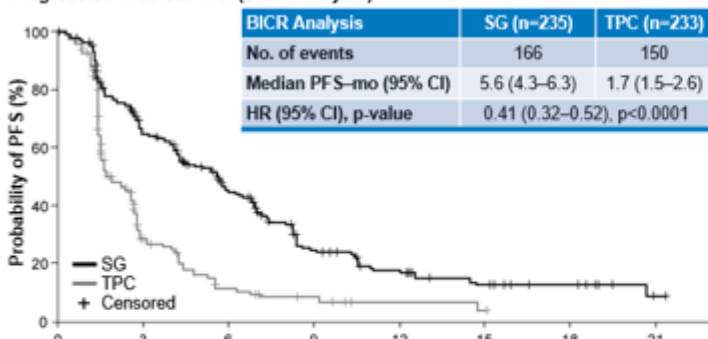


ASCENT was halted early due to compelling evidence of efficacy per unanimous DSMC recommendation. Here, we report the primary results from ASCENT, including PFS and OS.



ASCENT Results

Progression-Free Survival (BICR Analysis)*

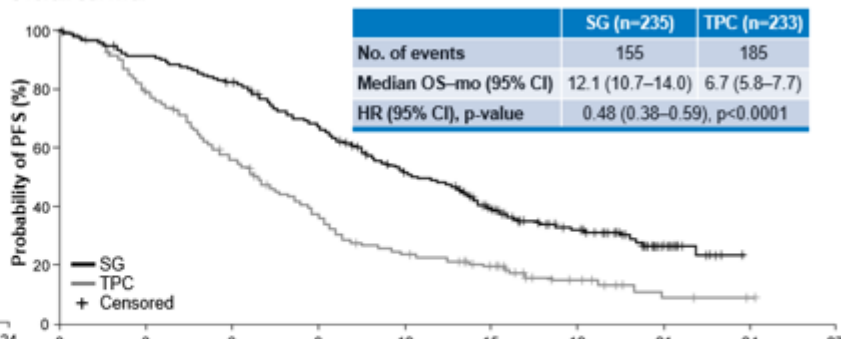


Number of patients at risk

Time (months)	0	3	6	9	12	15	18	21															
SG	235	222	166	134	127	104	81	63	54	37	33	24	22	16	15	13	9	8	8	5	3	1	0
TPC	233	179	78	35	32	19	12	9	7	6	4	2	2	2	2	1	0	0	0	0	0	0	0

PFS 5,6 vs. 1,7 Mon., HR 0,41
Δ +3,9 Monate

Overall Survival**



Number of patients at risk

Time (months)	0	3	6	9	12	15	18	21	24																	
SG	235	228	220	214	208	197	190	174	161	153	135	118	107	101	90	70	52	43	37	30	21	13	8	1	0	0
TPC	233	214	200	173	158	134	117	99	87	74	56	50	45	41	37	30	20	14	11	7	4	3	3	2	1	0

OS 12,1 vs. 6,7 Mon., HR 0,48
Δ +5,4 Monate

ASCENT Tox

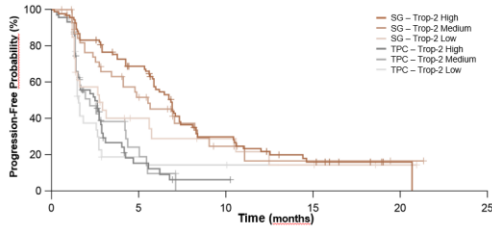
TRAE*		SG (n=258)			TPC (n=224)		
		All grade %	Grade 3, %	Grade 4, %	All grade %	Grade 3, %	Grade 4, %
Hematologic	Neutropenia [†]	63	46	17	43	27	13
	Anemia [‡]	34	8	0	24	5	0
	Leukopenia [§]	16	10	1	11	5	1
	Febrile neutropenia	6	5	1	2	2	<1
Gastrointestinal	Diarrhea	59	10	0	12	<1	0
	Nausea	57	2	<1	26	<1	0
	Vomiting	29	1	<1	10	<1	0
Other	Fatigue	45	3	0	30	5	0
	Alopecia	46	0	0	16	0	0

- Key grade ≥ 3 TRAEs (SG vs. TPC): neutropenia (51% vs. 33%), diarrhea (10% vs. <1%), leukopenia (10% vs. 5%), anemia (8% vs. 5%), and febrile neutropenia (6% vs. 2%)
 - G-CSF usage was 49% in the SG arm vs. 23% in the TPC arm
 - Dose reductions due to TRAEs were similar (22% SG vs. 26% TPC)
- No severe cardiovascular toxicity, no grade >2 neuropathy or grade >3 interstitial lung disease with SG
- No treatment-related deaths with SG; 1 treatment-related death (neutropenic sepsis) with TPC
- AEs leading to treatment discontinuation were low for SG and TPC: 4.7% and 5.4%
- Patients received a median of 7 treatment cycles of SG, with a median treatment duration of 4.4 months (range, 0.03–22.9)

ASCENT Effektivität nach Trop 2 Expression

ASCENT – Efficacy

Progression-Free Survival by Trop-2 Expression

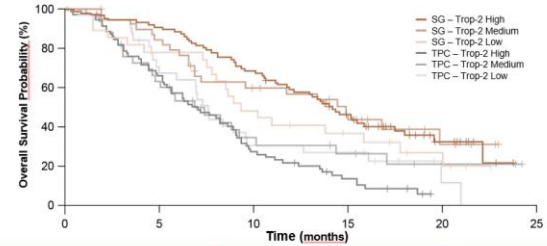


	Trop-2 High H-score: 200–300		Trop-2 Medium H-score: 100–200		Trop-2 Low H-score: <100	
	SG (n=85)	TPC (n=72)	SG (n=39)	TPC (n=35)	SG (n=27)	TPC (n=32)
Median PFS-mo (95% CI)	6.9 (5.8–7.4)	2.5 (1.5–2.9)	5.6 (2.9–8.2)	2.2 (1.4–4.3)	2.7 (1.4–5.8)	1.6 (1.4–2.7)

Assessed in brain metastases-negative population. Trop-2 expression determined in archival samples by validated immunohistochemistry assay and H-scoring. H-score, histochemical score; PFS, progression-free survival; SG, Sacituzumab Govitecan; TPC, treatment of physician's choice; Trop-2, trophoblast cell surface antigen-2.

ASCENT – Efficacy

Overall Survival by Trop-2 Expression



	Trop-2 High H-score: 200–300		Trop-2 Medium H-score: 100–200		Trop-2 Low H-score: <100	
	SG (n=85)	TPC (n=72)	SG (n=39)	TPC (n=35)	SG (n=27)	TPC (n=32)
Median OS-mo (95% CI)	14.2 (11.3–17.5)	6.9 (5.3–8.9)	14.9 (6.9-NE)	6.9 (4.6–10.1)	9.3 (7.5–17.8)	7.6 (5.0–9.6)

Assessed in brain metastases-negative population. Trop-2 expression determined in archival samples by validated immunohistochemistry assay and H-scoring. H-score, histochemical score; OS, overall survival; SG, Sacituzumab Govitecan; TPC, treatment of physician's choice; Trop-2, trophoblast cell surface antigen-2.

Triple negatives met. Mammakarzinom

- **Fazit aus 2020 für metastasiertes triple negatives Mammakarzinom**
 - 1. Immunonkologie bestätigt sich. Bisläng unklar warum manche CTX backbones in Kombination mit den IO klappen, andere nicht, noch keine Pembroluzassung**
 - 2. SG echte Chance für weitere Linie; Zulassung ?**



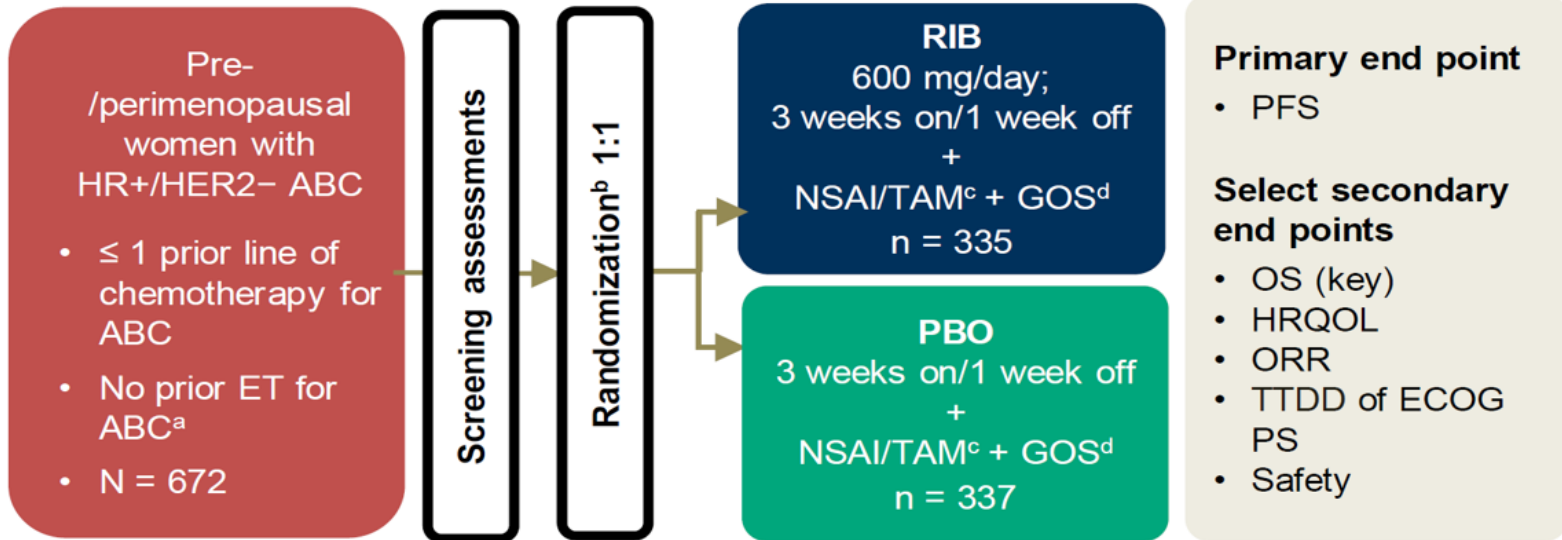
Metastasiertes Mammakarzinom Review of the year 2020

■ HR positives met. Mammakarzinom

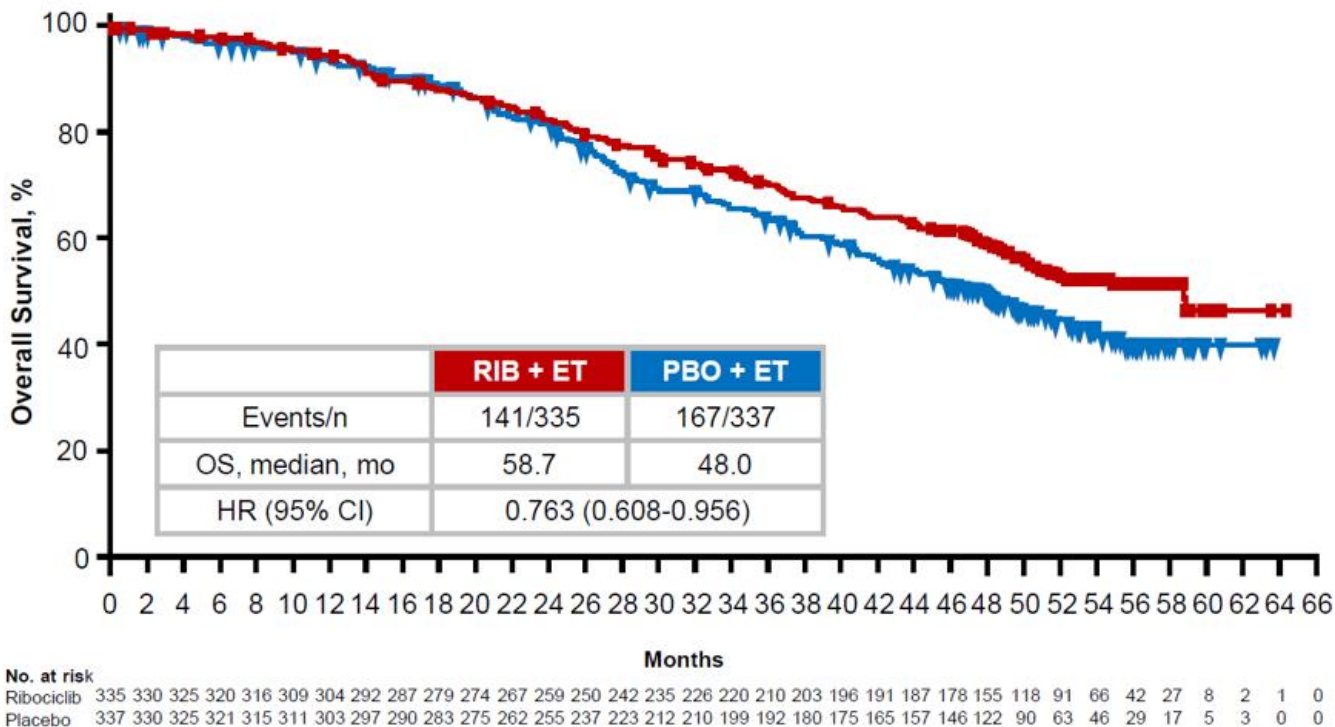
1) Updated OS-Daten MonaLeesa7

2) Alpelisib Bylieve

MONALEESA 7 Design

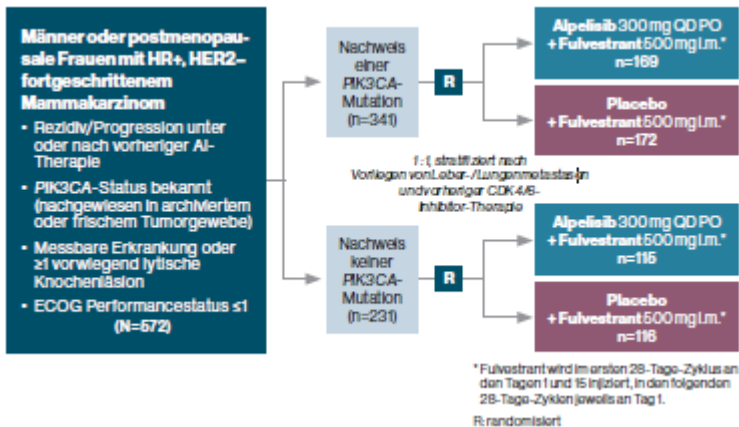


MONALEESA 7 OS ITT

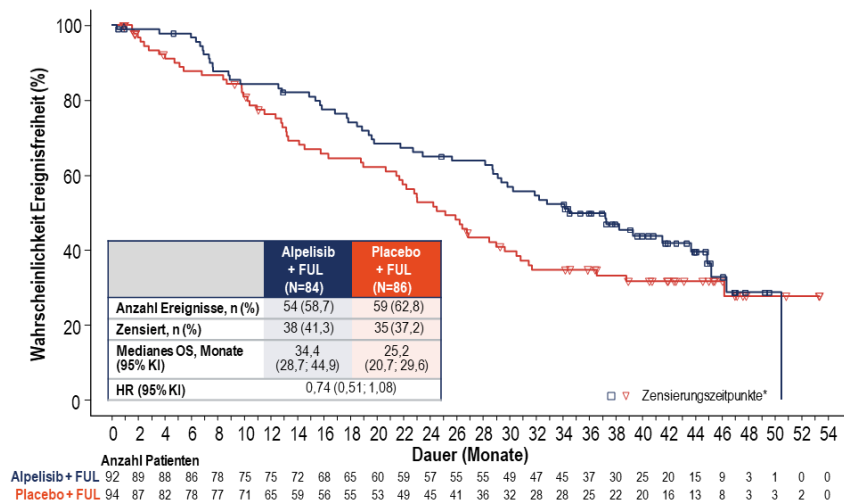


HR pos met. Mammakarzinom

SOLAR1 Design



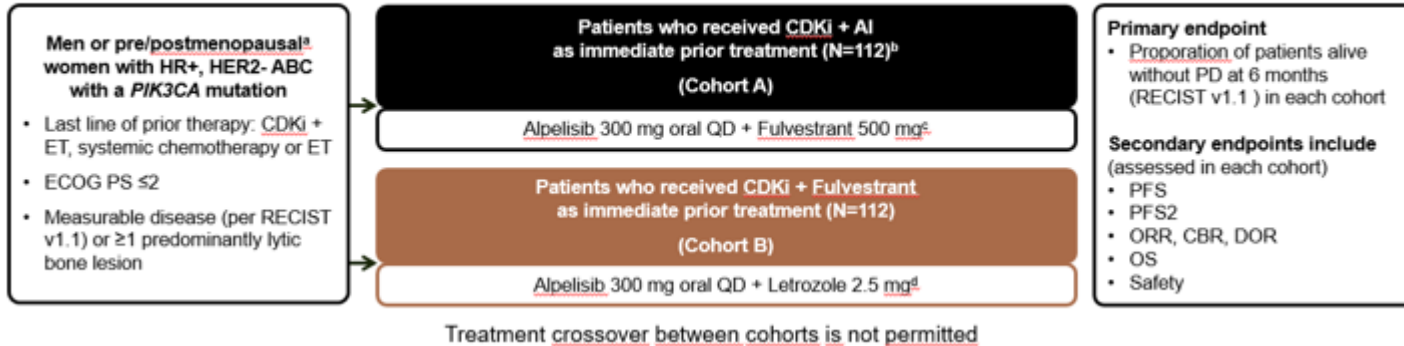
SOLAR1 OS



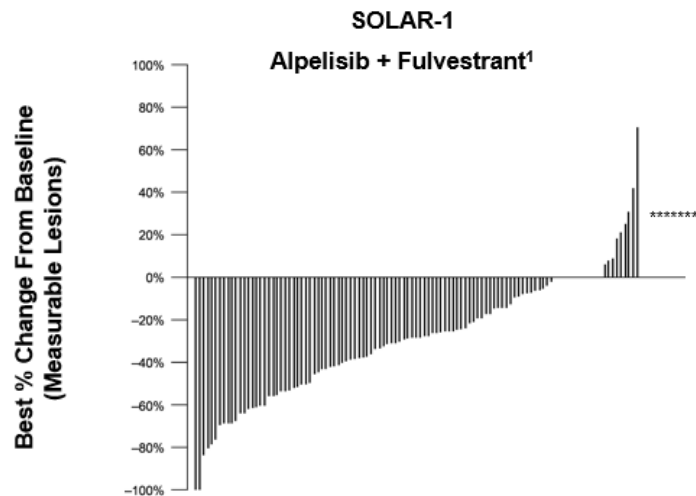
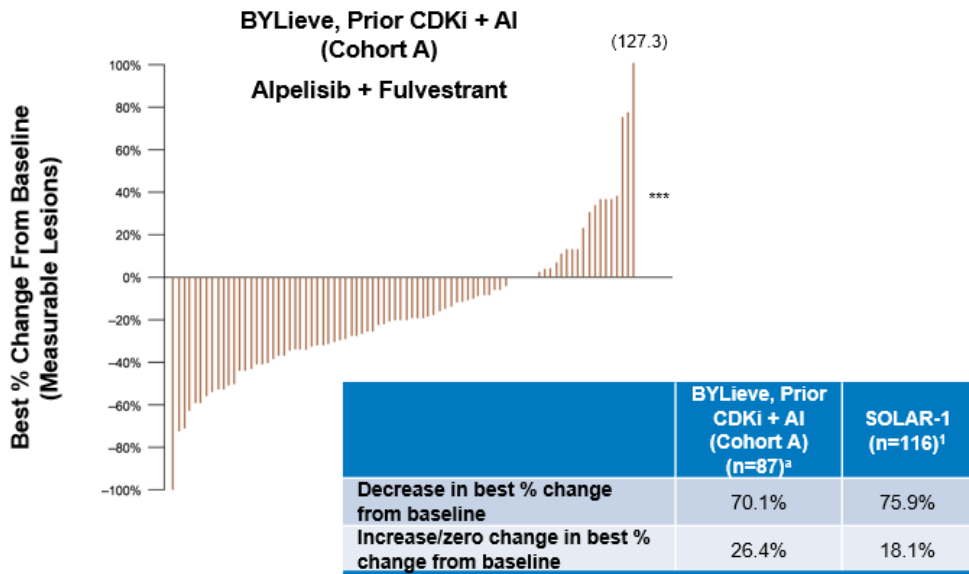
Zulassung für Alpelisib in Kombi mit Fulvestrant nach Progress unter AI

BYLIEVE Design

- **Goal:** In the post-CDKi setting, assess the efficacy and safety of Alpelisib + ET (Fulvestrant or Letrozole) in patients with PIK3CA-mutated HR+, HER2-ABC



Vergleich BYLIEVE uns SOLAR



SOLAR-1 data cutoff date: June 12, 2018; BYLieve data cutoff date: December 17, 2019. *Best percentage change in sum of diameters per investigator assessment, for patients with measurable disease at baseline. ^aPatients with missing best percentage change or those with best percentage change in target lesion but overall response of Unknown are excluded¹.
1. Reprinted from Juric D, et al. SABCS 2018. Abstract GS3-08 (oral).

HR positives met. Mammakarzinom

- **Fazit aus 2020 für metastasiertes HR positives Mammakarzinom**
 - 1. Bestätigung des Stellenwertes der CDK4/6 Inhibitoren (OS Vorteil für Ribociclib in der Monaleesa7)**
 - 2. Alpelisib funktioniert nach CDK4/6 Inhibitoren**



Review 2020-Ausblick 2021

- **Wünsche 2021**
 - Corona ist wieder ein Bier
 - Positiv ist wieder was positives
 - Tests werden in der Schule gemacht
 - Isolierung ist etwas für Hauswände und Kabel
 - Mit einer Maske wird Karneval gefeiert
-
- Donald ist wieder eine lustige Ente

Review 2020-Ausblick 2021

- **Wünsche 2021**
 - Corona ist wieder ein Bier
 - Positiv ist wieder was positives
 - Tests werden in der Schule gemacht
 - Isolierung ist etwas für Hauswände und Kabel
 - Mit einer Maske wird Karneval gefeiert
-
- Donald ist wieder eine lustige Ente
 - Vielen Dank für Ihre/Eure Aufmerksamkeit

