Nouvelles thérapeutiques dans les cancers du sein

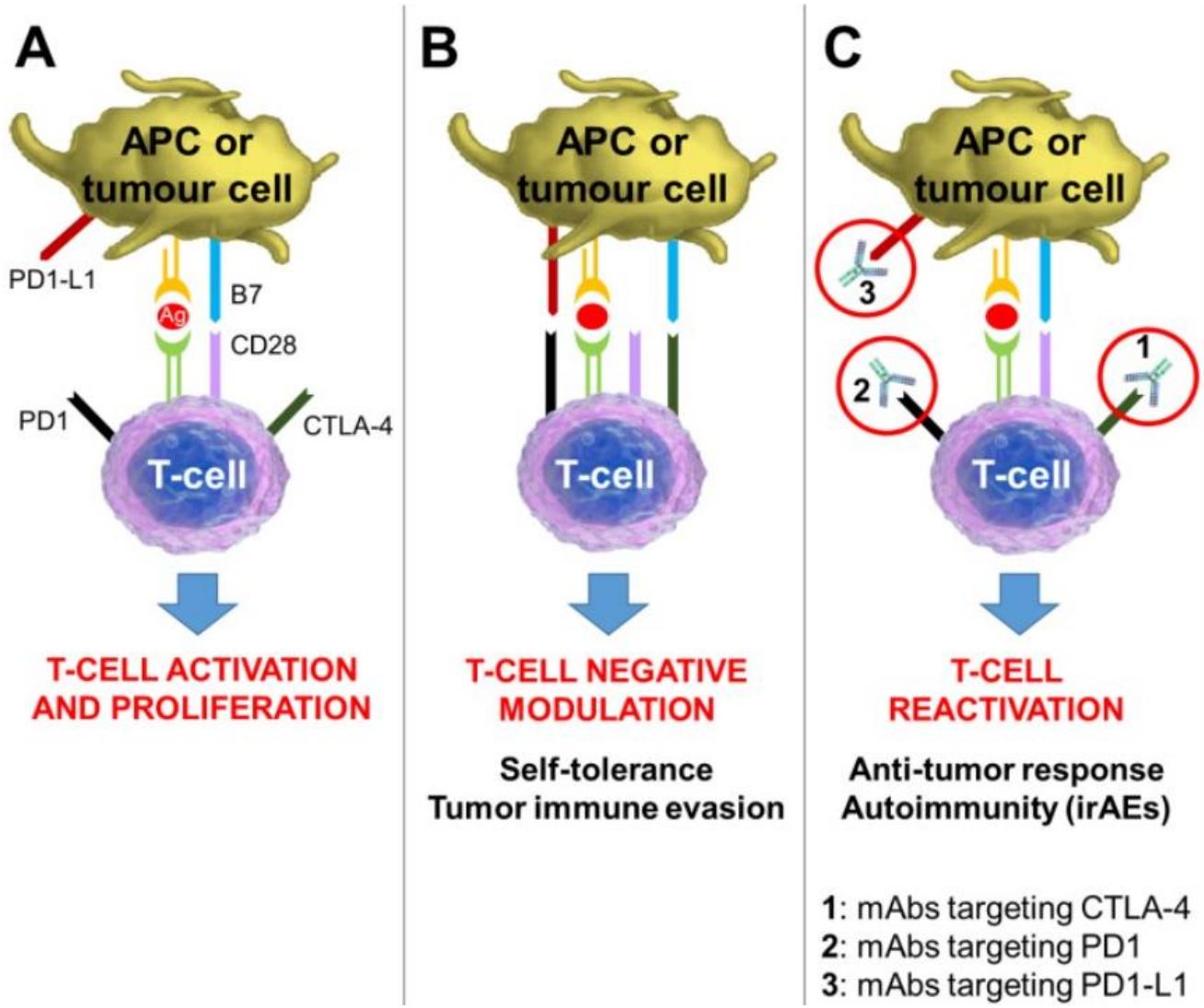
Journée des Formateurs

02/12/2022
Dole
Dr NIOGRET Julie

PEMBROLIZUMAB
KEYTRUDA®

Mécanisme d'action

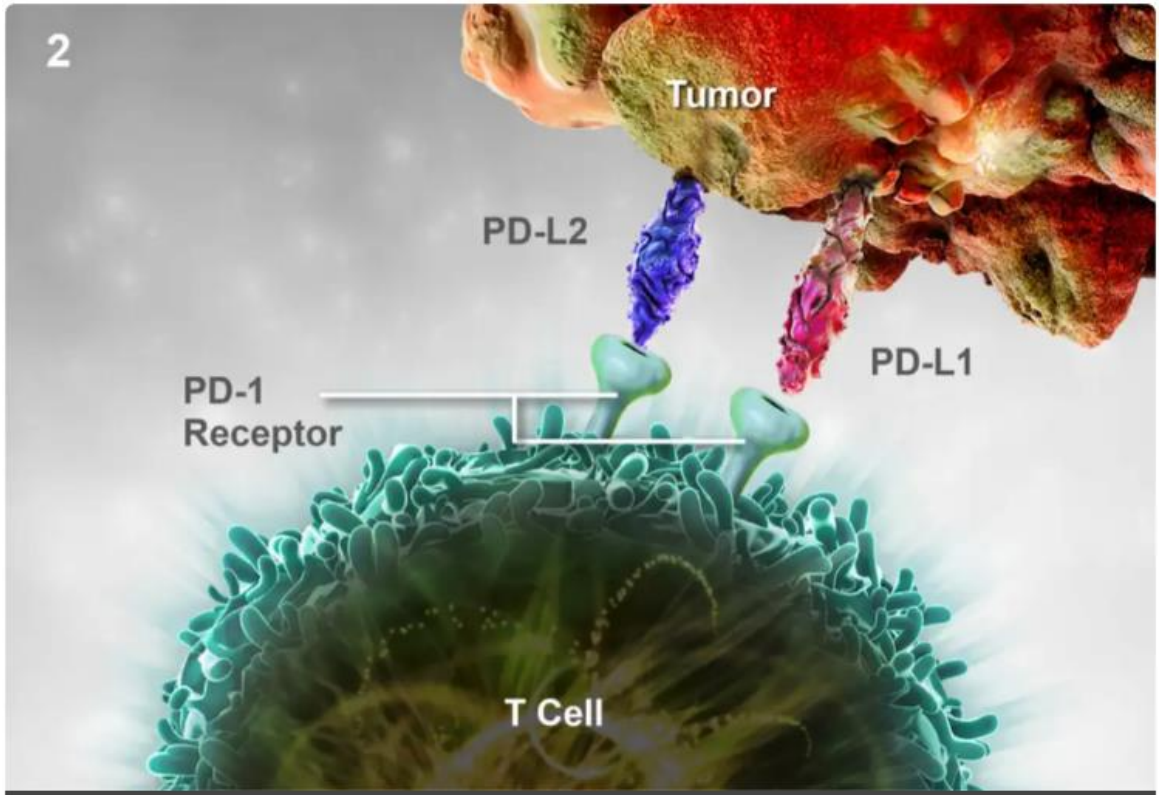
Immunothérapie



Feingold KR, Anawalt B, Boyce A, et al., editors. South Dartmouth (MA): MDText.com, Inc.; 2000-.

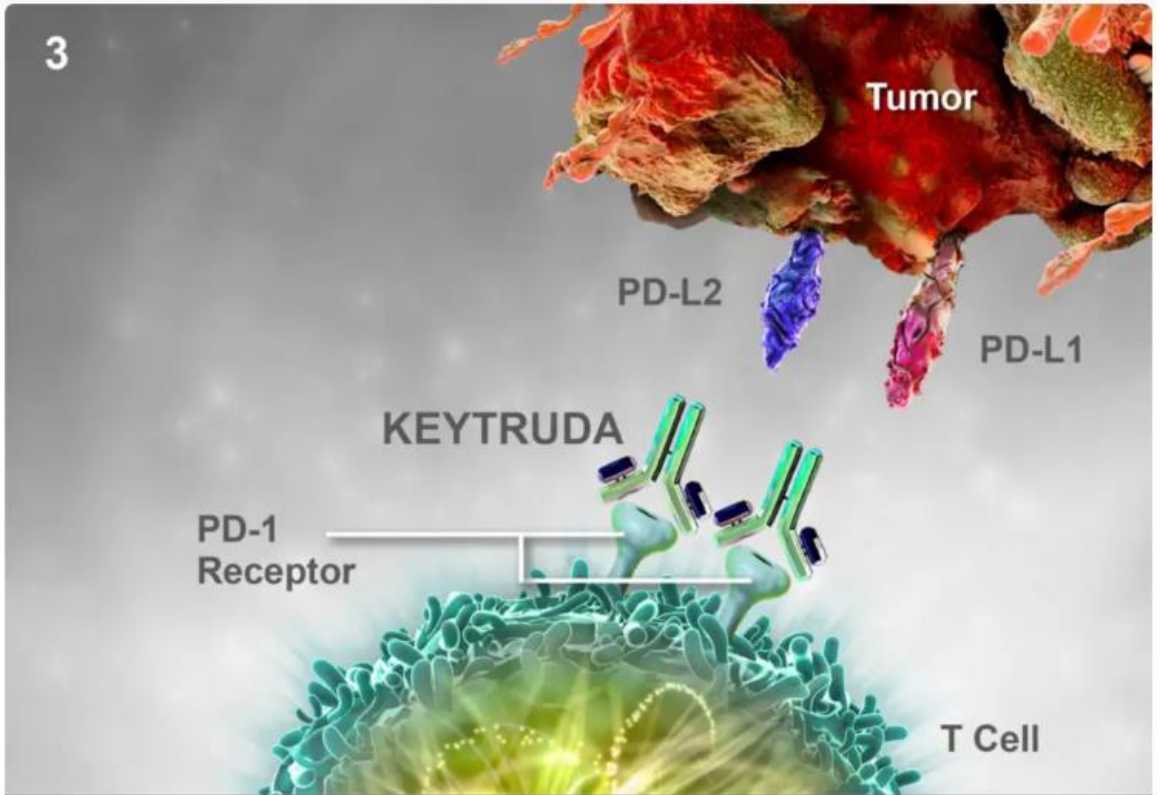
Mécanisme d'action

Pembrolizumab - Keytruda®



Tumor evasion and T-cell deactivation

Some tumors can evade the immune system through the PD-1 pathway. The PD-L1 and PD-L2 ligands on tumors can bind with PD-1 receptors on T cells to inactivate the T cells.



T-cell reactivation with KEYTRUDA

KEYTRUDA binds to the PD-1 receptor and blocks its interaction with PD-L1 and PD-L2, which helps restore the immune response. While having an effect on the tumor, this could also affect normal healthy cells.

https://www.keytrudahcp.com/resources/mechanism-of-action/.

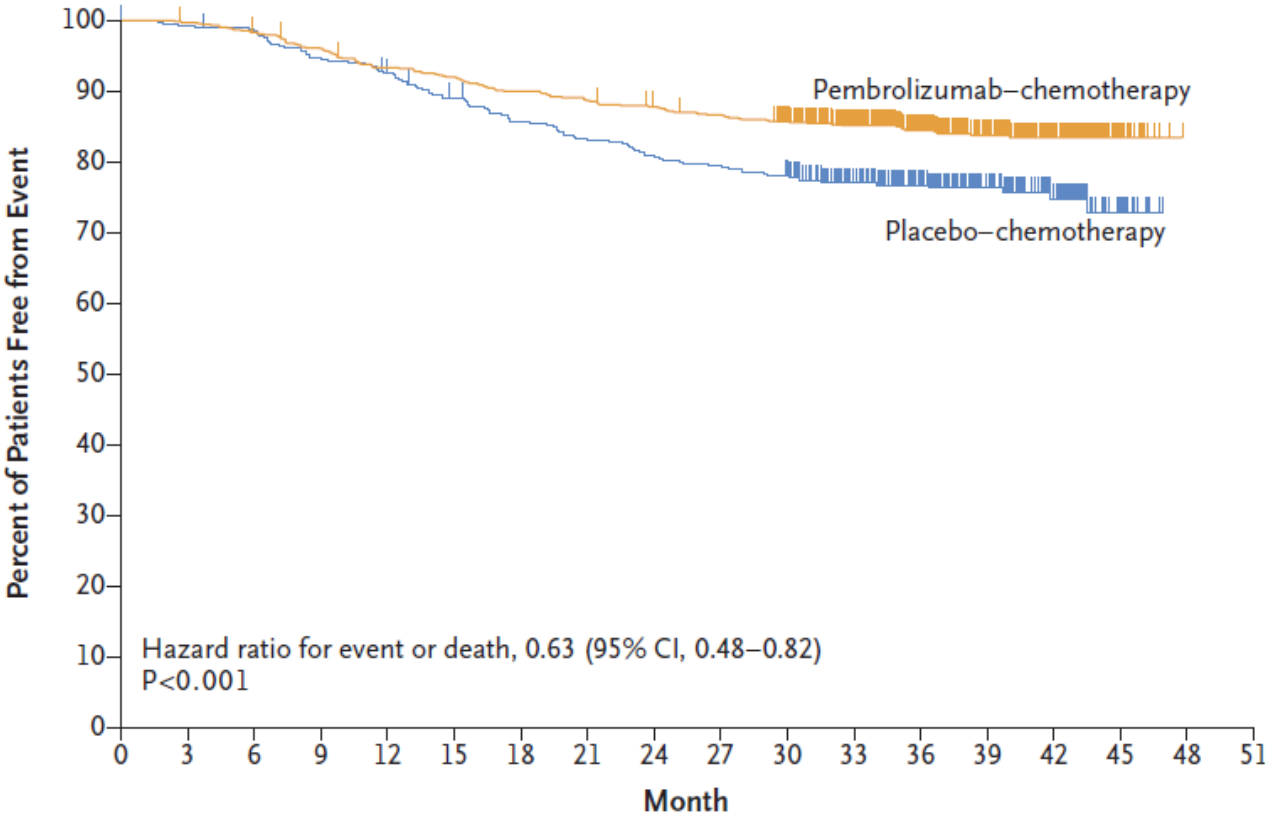
Efficacité

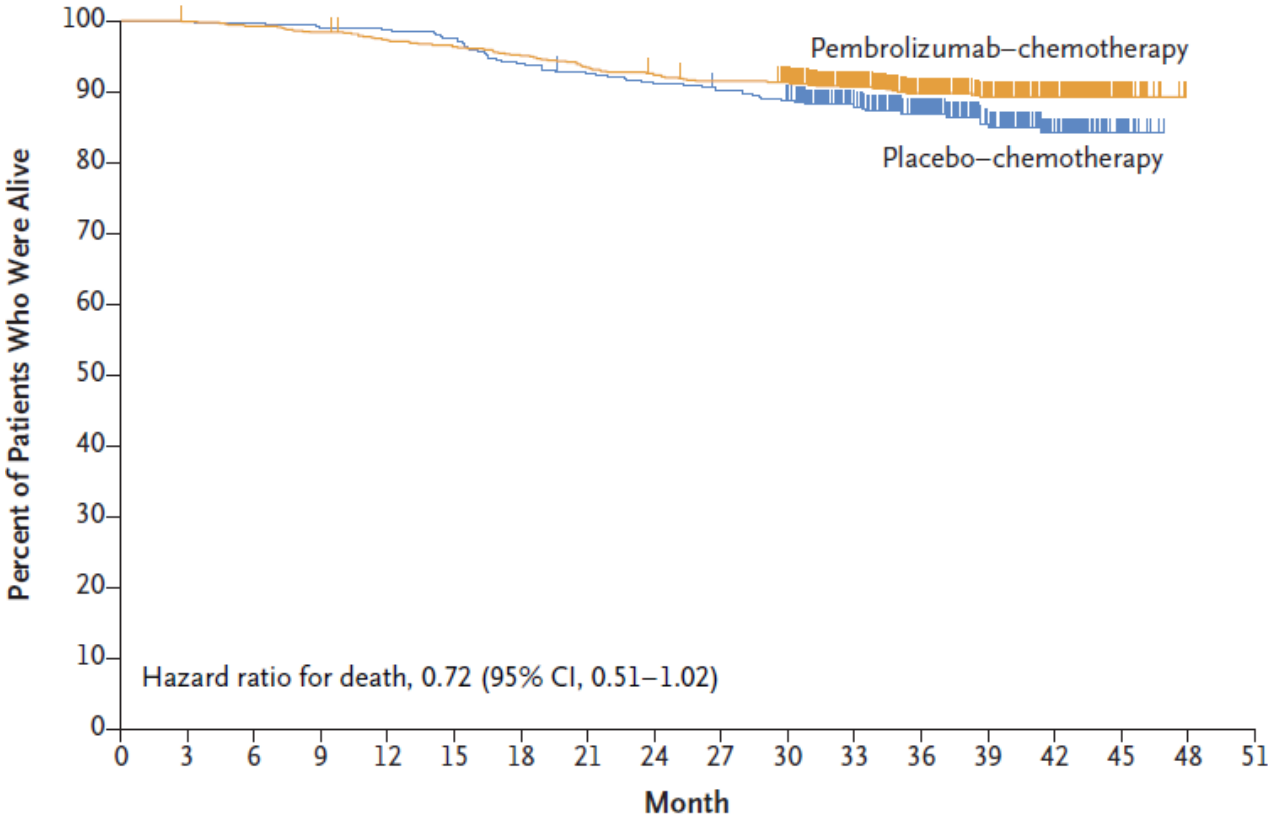
KEYNOTE 522

TBNC localisés non prétraités, situation néoadjuvante

Table 2. Pathological Complete Response, According to Pathological Stage.*

Variable	Pembrolizumab–Chemotherapy (N=401)	Placebo–Chemotherapy (N=201)	Estimated Treatment Difference†	P Value
			percentage points (95% CI)	
Pathological stage ypT0/Tis ypN0				
No. of patients	260	103		
Percentage of patients with response (95% CI)	64.8 (59.9–69.5)	51.2 (44.1–58.3)	13.6 (5.4–21.8)	P<0.001





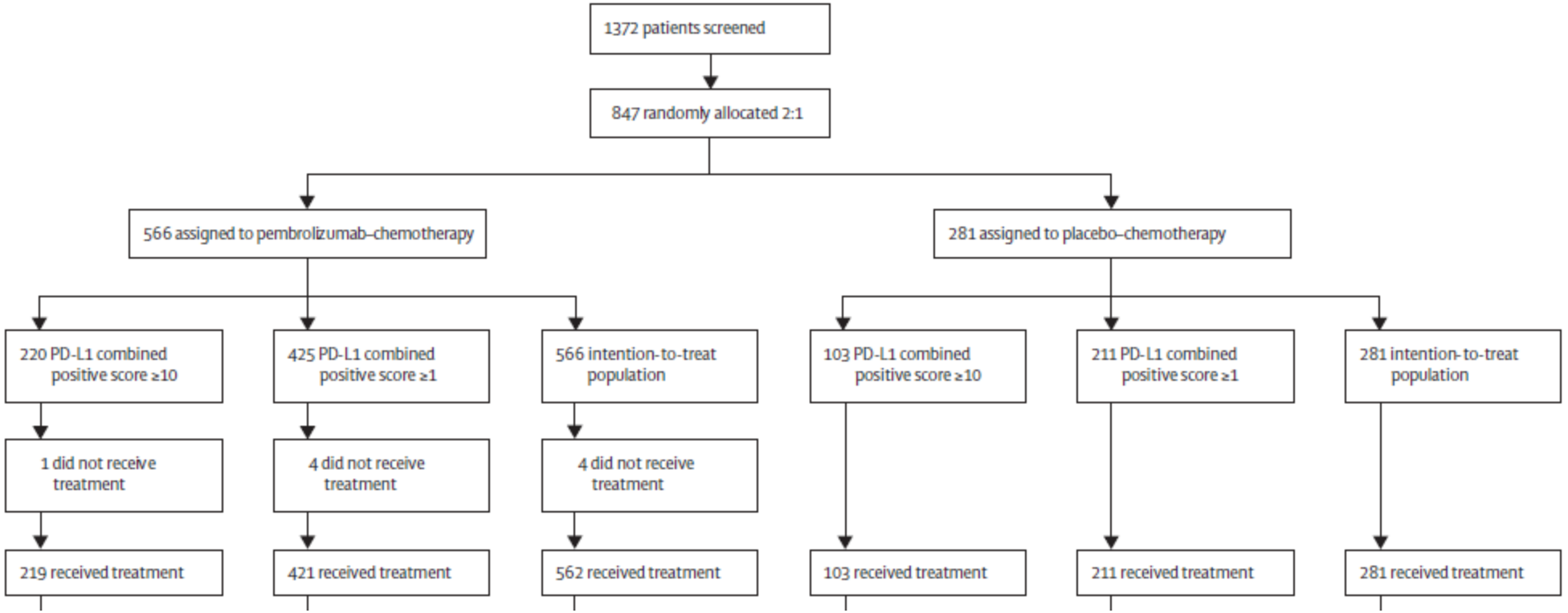
Schmid et al. N Engl J Med; 2020; 382:810-21

Schmid et al. N Engl J Med; 2022; 386:556-67

Efficacité

KEYNOTE 355

TBNC M+ ou récidive locale inopérable L1



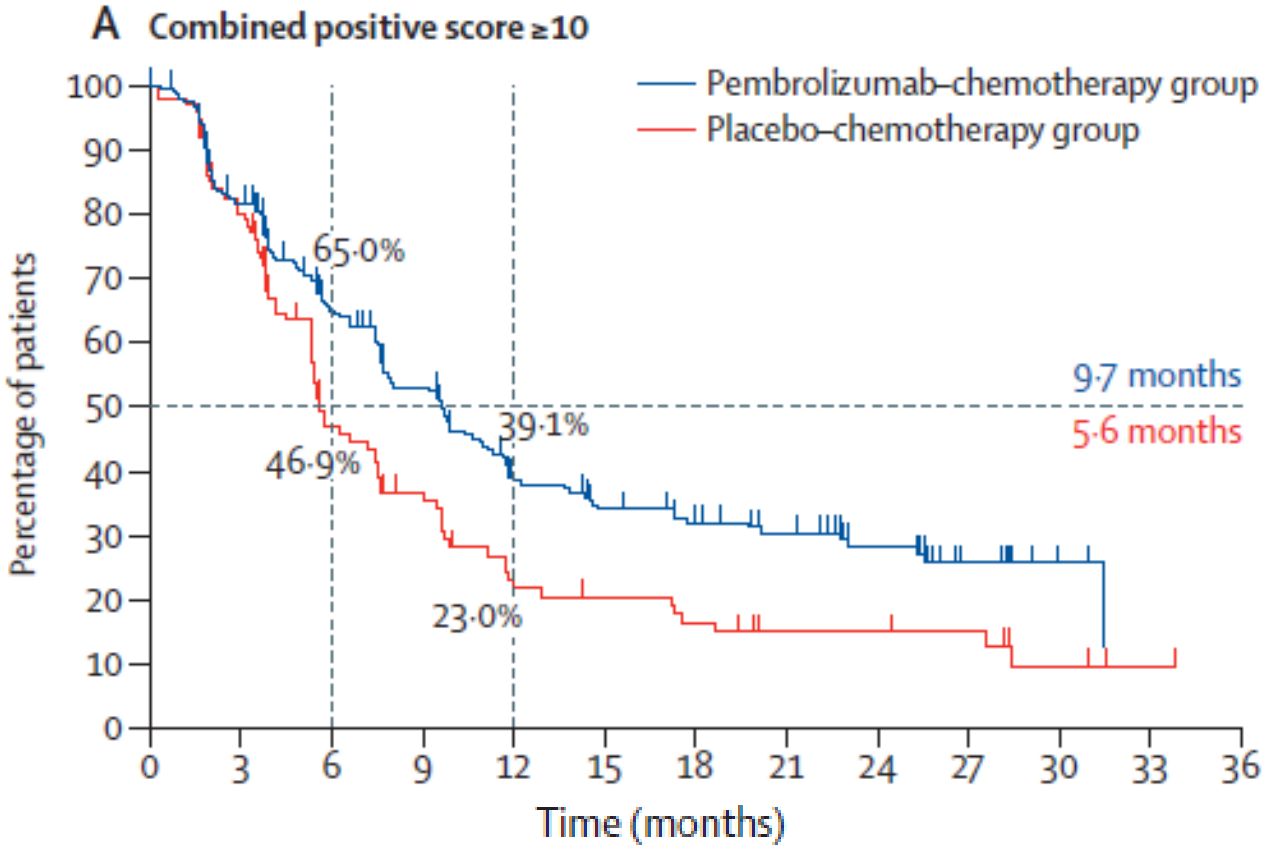
Stratification selon expression PD-L1 par la tumeur

Cortes et al. Lancet; 2020; 396:1817-28

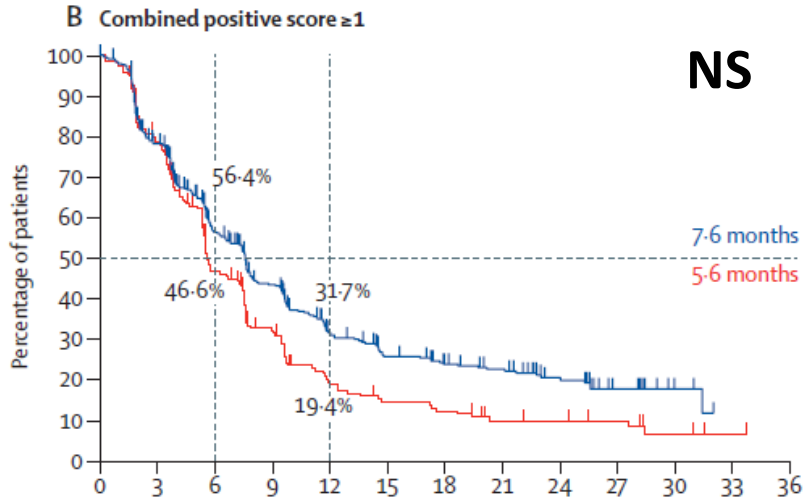
Efficacité

KEYNOTE 355

TBNC M+ ou récidive locale inopérable L1



HR = 0,65 IC95 [0,49 – 0,86] p=0,0012



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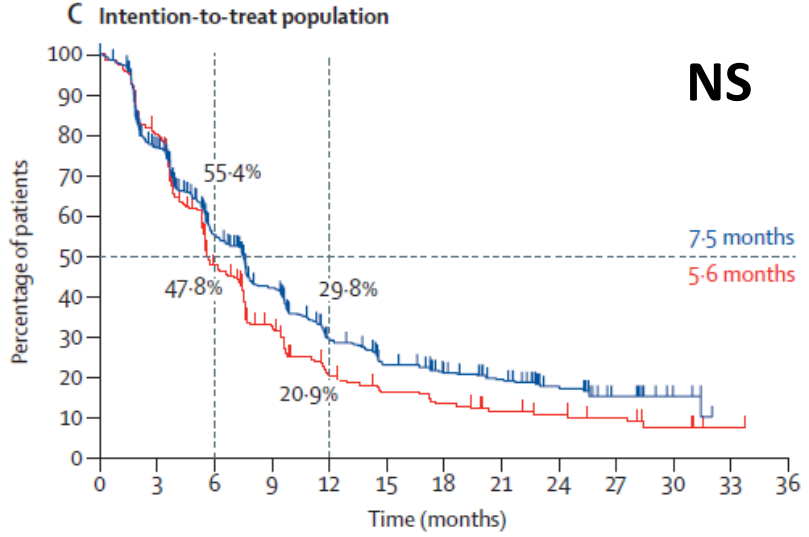

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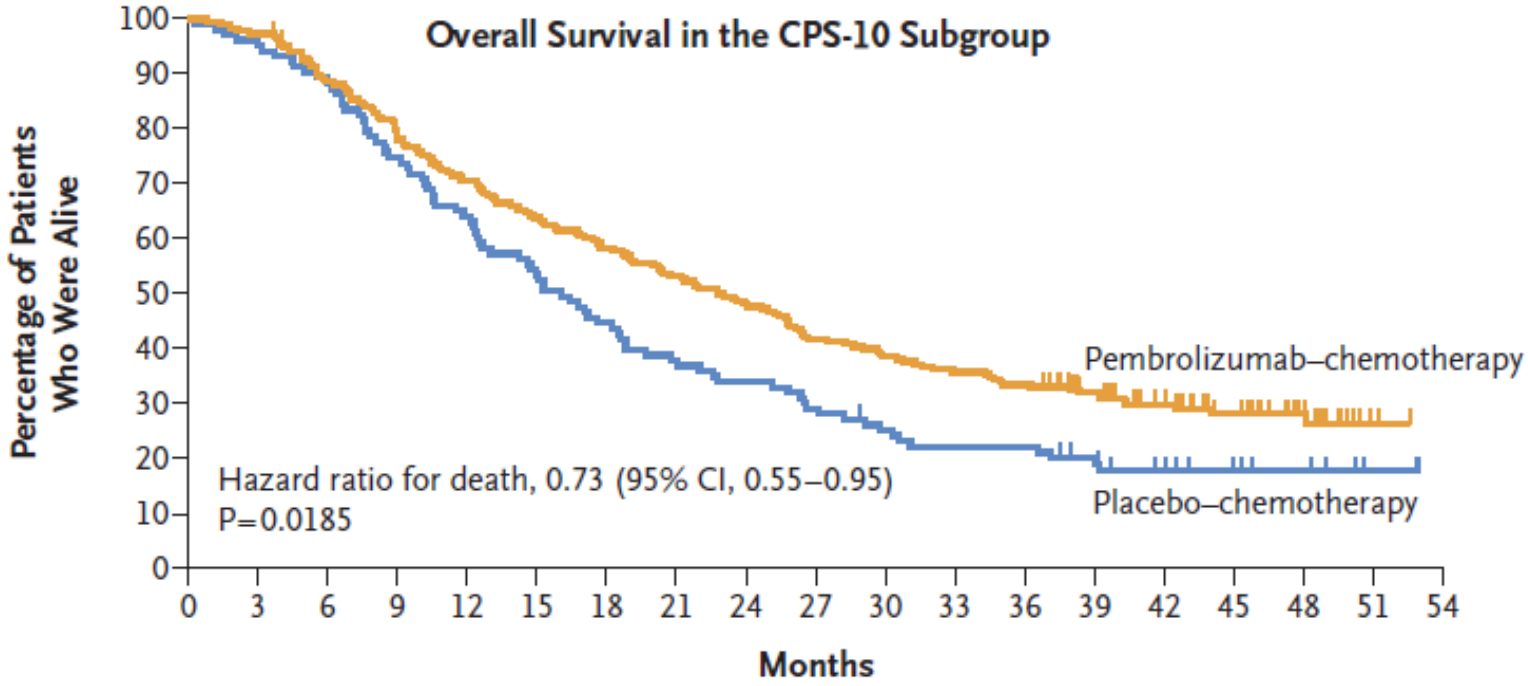
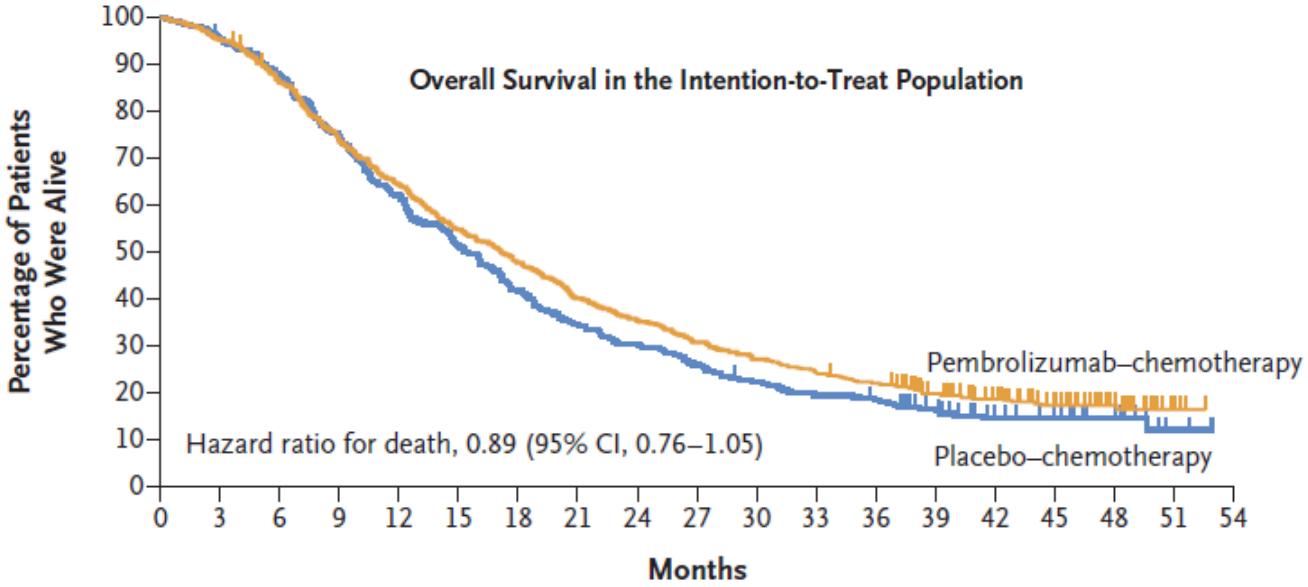
Cortes et al. Lancet; 2020; 396:1817-28

Efficacité

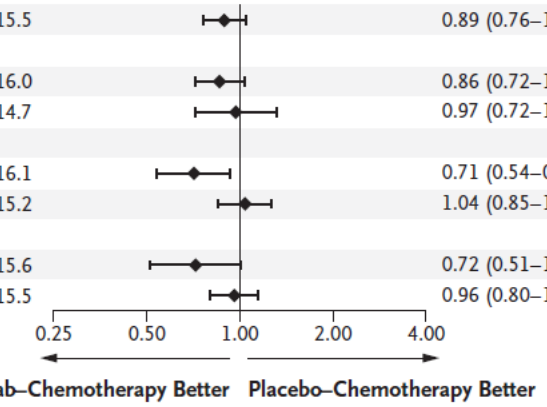
KEYNOTE 355

TBNC M+ ou récidivé locale inopérable L1





Subgroup	No. of Patients	Median Overall Survival (mo)		Hazard Ratio for Death (95% CI)
		Pembrolizumab–chemotherapy	Placebo–chemotherapy	
Overall	847	17.2	15.5	0.89 (0.76–1.05)
PD-L1 CPS cutoff of 1				
CPS ≥1	636	17.6	16.0	0.86 (0.72–1.04)
CPS <1	211	16.2	14.7	0.97 (0.72–1.32)
PD-L1 CPS cutoff of 10				
CPS ≥10	323	23.0	16.1	0.71 (0.54–0.93)
CPS <10	524	14.7	15.2	1.04 (0.85–1.26)
PD-L1 CPS cutoff of 20				
CPS ≥20	204	24.0	15.6	0.72 (0.51–1.01)
CPS <20	643	15.9	15.5	0.96 (0.80–1.14)



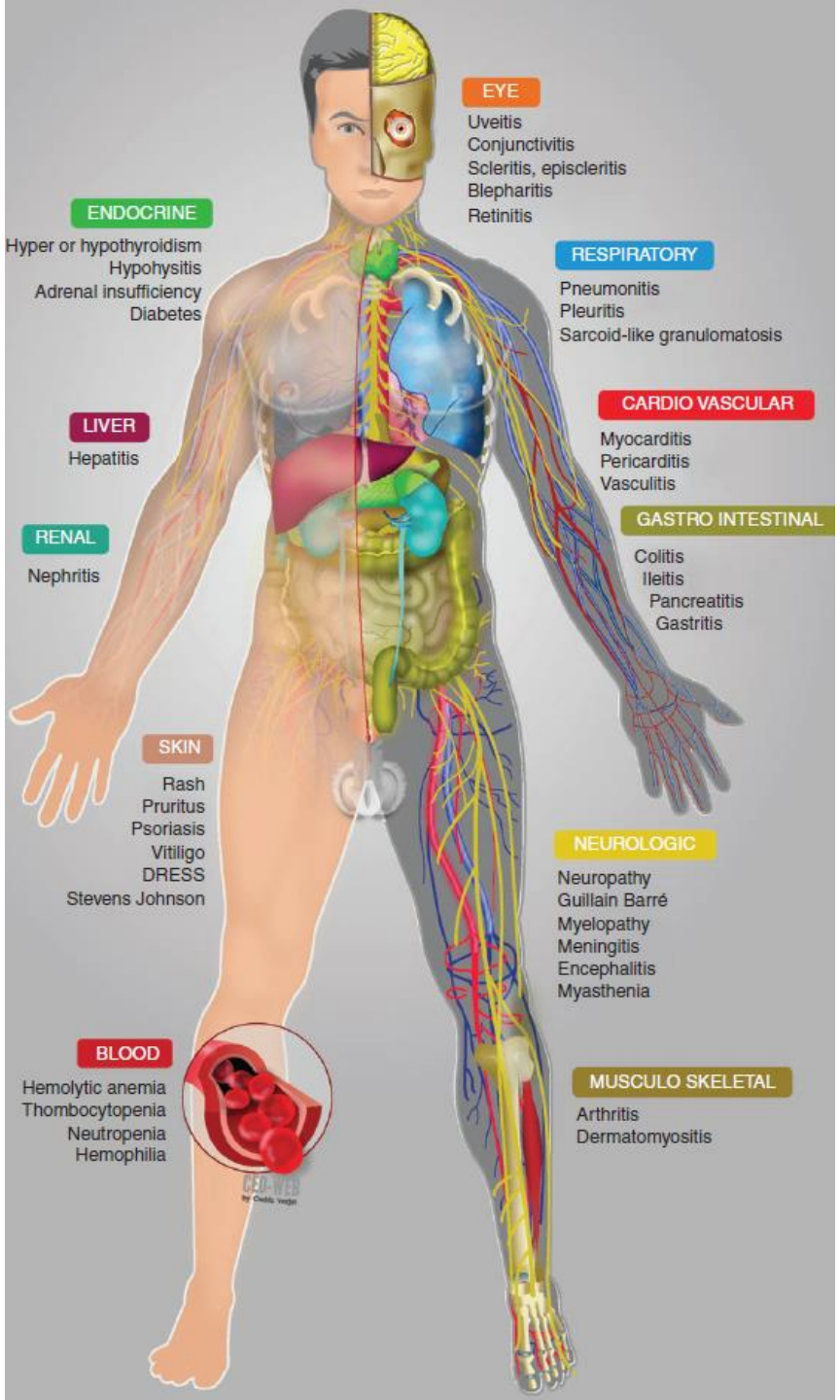
Cortes et al. N Engl J Med; 2022; 387:217-26

Tolérance

Table 1. Immune checkpoint blockade (ICB) toxicities

Frequent (>10%) ICB toxicities
- Ipilimumab (anti-CTLA4): diarrhea, rash, pruritus, fatigue, nausea, vomiting, decreased appetite and abdominal pain
- Nivolumab (anti-PD1): fatigue, rash, pruritus, diarrhea and nausea
- Pembrolizumab (anti-PD1): diarrhea, nausea, pruritus, rash, arthralgia and fatigue

Rare (<10%) life-threatening ICB toxicities
- Colitis and risk of gastrointestinal perforation
- Pneumonitis including acute interstitial pneumonia/acute respiratory distress syndrome
- Infusion reaction and anaphylactic shock
- Type 1 diabetes and risk of diabetic ketoacidosis
- Severe skin reactions, DRESS, Stevens Johnson syndrome
- Hemolytic anemia or immune thrombocytopenia and hemorrhagic risk
- Neutropenia and sepsis risk
- Encephalopathy and neurological sequelae
- Guillain–Barré syndrome and respiratory risk
- Myelitis and motor sequelae
- Myocarditis and cardiac insufficiency
- Acute adrenal insufficiency and hypovolemic shock
- Pleural and pericardial effusion
- Nephritis



Champiat et al. Annals of Oncology ,2016; 27:559-74

Tolérance

Event	Pembrolizumab–Chemotherapy (N = 781)		Placebo–Chemotherapy (N = 389)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
	number of patients (percent)			
Any adverse event	777 (99.5)	633 (81.0)	389 (100.0)	295 (75.8)
Treatment-related adverse event†	773 (99.0)	600 (76.8)	388 (99.7)	281 (72.2)
Nausea	490 (62.7)	26 (3.3)	246 (63.2)	5 (1.3)
Alopecia	471 (60.3)	14 (1.8)	220 (56.6)	8 (2.1)
Anemia	430 (55.1)	142 (18.2)	215 (55.3)	58 (14.9)
Neutropenia	365 (46.7)	270 (34.6)	183 (47.0)	129 (33.2)
Fatigue	321 (41.1)	27 (3.5)	147 (37.8)	6 (1.5)
Diarrhea	230 (29.4)	17 (2.2)	92 (23.7)	5 (1.3)
Elevated alanine aminotransferase level	199 (25.5)	41 (5.2)	96 (24.7)	9 (2.3)
Vomiting	199 (25.5)	18 (2.3)	85 (21.9)	6 (1.5)
Asthenia	191 (24.5)	25 (3.2)	99 (25.4)	9 (2.3)
Constipation	185 (23.7)	0	82 (21.1)	0
Decreased neutrophil count	185 (23.7)	146 (18.7)	112 (28.8)	90 (23.1)
Rash	170 (21.8)	7 (0.9)	59 (15.2)	1 (0.3)
Peripheral neuropathy	154 (19.7)	15 (1.9)	82 (21.1)	4 (1.0)
Adverse event of interest‡	304 (38.9)	101 (12.9)	71 (18.3)	7 (1.8)
Infusion reaction	132 (16.9)	20 (2.6)	43 (11.1)	4 (1.0)
Hypothyroidism	107 (13.7)	3 (0.4)	13 (3.3)	0
Hyperthyroidism	36 (4.6)	2 (0.3)	4 (1.0)	0
Severe skin reaction	34 (4.4)	30 (3.8)	4 (1.0)	1 (0.3)
Adrenal insufficiency	18 (2.3)	10 (1.3)	0	0

Event	Pembrolizumab–Chemotherapy (N = 562)		Placebo–Chemotherapy (N = 281)	
	Any Grade	Grade 3, 4, or 5	Any Grade	Grade 3, 4, or 5
	number of patients (percent)			
Any adverse event	554 (98.6)	438 (77.9)	276 (98.2)	207 (73.7)
Adverse events that were attributed to the trial regimen†	541 (96.3)	383 (68.1)	267 (95.0)	188 (66.9)
Anemia	276 (49.1)	93 (16.5)	129 (45.9)	41 (14.6)
Neutropenia	231 (41.1)	167 (29.7)	107 (38.1)	84 (29.9)
Nausea	221 (39.3)	9 (1.6)	116 (41.3)	4 (1.4)
Alopecia	186 (33.1)	5 (0.9)	94 (33.5)	3 (1.1)
Fatigue	161 (28.6)	16 (2.8)	84 (29.9)	7 (2.5)
Neutrophil count decreased	126 (22.4)	98 (17.4)	74 (26.3)	57 (20.3)
Alanine aminotransferase increased	115 (20.5)	34 (6.0)	46 (16.4)	13 (4.6)
Immune-mediated adverse events‡	149 (26.5)	30 (5.3)	18 (6.4)	0
Hypothyroidism	89 (15.8)	2 (0.4)	9 (3.2)	0
Hyperthyroidism	24 (4.3)	1 (0.2)	3 (1.1)	0
Pneumonitis	14 (2.5)	6 (1.1)	0	0
Colitis	10 (1.8)	2 (0.4)	4 (1.4)	0
Severe skin reactions	10 (1.8)	10 (1.8)§	1 (0.4)	0

Schmid et al. N Engl J Med; 2020; 382:810-21

Cortes et al. N Engl J Med; 2022; 387:217-26

Indications

HAUTE AUTORITÉ DE SANTÉ

ATU

Autorisation d'accès précoce octroyée le 17 mars 2022 à la spécialité KEYTRUDA (pembrolizumab) dans l'indication « en association à une chimiothérapie comme traitement néoadjuvant, puis poursuivi après la chirurgie en monothérapie comme traitement adjuvant, dans le traitement des patients adultes atteints d'un cancer du sein triple négatif localement avancé, inflammatoire ou de stade précoce à haut risque de récidive ».

AMM

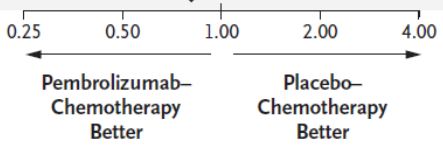
KEYTRUDA (pembrolizumab) en association à une chimiothérapie, est un traitement de première ligne du cancer du sein triple négatif localement récurrent non résécable ou métastatique, dont les tumeurs expriment PD-L1 avec un CPS ≥ 10.

Faute de comparaison, la place de cette association en première ligne par rapport aux inhibiteurs de PARP en cas de tumeur avec mutation BRCA1/2, reste à déterminer.

Schmid et al. N Engl J Med; 2022; 386:556-67

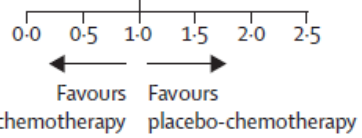
Données chez les personnes âgées

Subgroup	Pembrolizumab–Chemotherapy	Placebo–Chemotherapy	Hazard Ratio for Event or Death (95% CI)
	no. of patients with event/total no. (%)		
Overall	123/784 (15.7)	93/390 (23.8)	0.63 (0.48–0.82)
Nodal status			
Positive	80/408 (19.6)	57/196 (29.1)	0.65 (0.46–0.91)
Negative	43/376 (11.4)	36/194 (18.6)	0.58 (0.37–0.91)
Tumor size			
T1 to T2	64/581 (11.0)	59/290 (20.3)	0.51 (0.36–0.73)
T3 to T4	59/203 (29.1)	34/100 (34.0)	0.84 (0.55–1.28)
Carboplatin schedule			
Weekly	71/444 (16.0)	56/220 (25.5)	0.60 (0.42–0.86)
Every 3 wk	50/334 (15.0)	37/167 (22.2)	0.65 (0.42–0.99)
PD-L1 status			
Positive	98/656 (14.9)	68/317 (21.5)	0.67 (0.49–0.92)
Negative	25/128 (19.5)	25/69 (36)	0.48 (0.28–0.85)
Age			
<65 yr	103/700 (14.7)	79/342 (23.1)	0.61 (0.45–0.82)
≥65 yr	20/84 (24)	14/48 (29)	0.79 (0.40–1.56)
ECOG performance-status score			
0	101/678 (14.9)	80/341 (23.5)	0.60 (0.45–0.80)
1	22/106 (20.8)	13/49 (27)	0.81 (0.41–1.62)



Schmid et al. N Engl J Med; 2022; 386:556-67

	n	Median, months: Pembrolizumab-chemotherapy	Median, months: Placebo-chemotherapy	Hazard ratio for progression or death (95% CI)
B Combined positive score ≥10				
Age, years				
<65	257	9·5	5·5	0·63 (0·46 to 0·87)
≥65	66	10·7	7·6	0·67 (0·37 to 1·23)
Geographical region				
North America-Europe-Australia and New Zealand	212	9·6	5·7	0·69 (0·49 to 0·97)
Asia	56	17·3	5·6	0·45 (0·22 to 0·91)
Rest of world	55	7·6	6·2	0·65 (0·40 to 1·55)
Eastern Cooperative Oncology Group performance status				
0	196	9·8	7·5	0·74 (0·51 to 1·07)
1	127	7·6	3·9	0·50 (0·33 to 0·78)
On-study chemotherapy				
Nab-paclitaxel	99	9·9	5·5	0·57 (0·34 to 0·95)
Paclitaxel	44	9·6	3·6	0·33 (0·14 to 0·76)
Gemcitabine-carboplatin	180	8·0	7·2	0·77 (0·53 to 1·11)
Previous same class chemotherapy				
Yes	65	7·5	5·4	0·60 (0·32 to 1·15)
No	258	9·9	5·7	0·66 (0·48 to 0·90)
Previous neoadjuvant or adjuvant chemotherapy				
Yes	193	7·9	5·7	0·78 (0·55 to 1·12)
No	130	11·0	5·4	0·47 (0·30 to 0·74)
Disease-free interval				
De novo metastasis	103	9·7	5·3	0·48 (0·29 to 0·79)
<12 months	66	7·5	7·2	1·00 (0·51 to 1·95)
≥12 months	153	9·9	6·6	0·64 (0·43 to 0·95)
Number of metastatic sites				
<3	184	11·8	9·0	0·68 (0·46 to 1·00)
≥3	138	7·6	4·5	0·52 (0·34 to 0·78)
Overall	**323**	**9·7**	**5·6**	**0·65 (0·49 to 0·86)**



Cortes et al. Lancet; 2020; 396:1817-28

Données chez les personnes âgées

	Age ≥75 Years, n = 149				Age < 75 Years, n = 1323			
	Any		Grade ≥3		Any		Grade ≥3	
Treatment-related AEs	**102**	**(68.5)**	**36**	**(24.2)**	**862**	**(65.2)**	**224**	**(16.9)**
Serious	24	(16.1)	20	(13.4)	170	(12.8)	137	(10.4)
Led to discontinuation	16	(10.7)	10	(6.7)	90	(6.8)	73	(5.5)
Led to death[b]	2	(1.3)	2	(1.3)	17	(1.3)	17	(1.3)
Occurring in > 10% of patients in any group								
Fatigue	26	(17.4)	3	(2.0)	140	(10.6)	13	(1.0)
Decreased appetite	19	(12.8)	1	(0.7)	119	(9.0)	9	(0.7)
Pruritus	19	(12.8)	1	(0.7)	106	(8.0)	3	(0.2)
Rash	18	(12.1)	2	(1.3)	119	(9.0)	4	(0.3)
Nausea	14	(9.4)	1	(0.7)	103	(7.8)	2	(0.2)
Diarrhea	9	(6.0)	1	(0.7)	102	(7.7)	12	(0.9)
Anemia	7	(4.7)	1	(0.7)	62	(4.7)	11	(0.8)
Asthenia	4	(2.7)	1	(0.7)	73	(5.5)	6	(0.5)
Constipation	3	(2.0)	0		34	(2.6)	0	
Vomiting	3	(2.0)	0		43	(3.3)	2	(0.2)
Platelet count decreased	1	(0.7)	0		4	(0.3)	1	(0.1)
Thrombocytopenia	1	(0.7)	0		7	(0.5)	2	(0.2)
WBC count decreased	1	(0.7)	0		5	(0.4)	0	
Alopecia	0		0		9	(0.7)	0	
Neutropenia	0		0		8	(0.6)	1	(0.1)
Neutrophil count decreased	0		0		5	(0.4)	0	
Immune-mediated AEs and infusion reactions	**37**	**(24.8)**	**14**	**(9.4)**	**331**	**(25.0)**	**94**	**(7.1)**
Hypothyroidism	13	(8.7)	0		138	(10.4)	1	(0.1)
Pneumonitis	11	(7.4)	4	(2.7)	90	(6.8)	39	(2.9)
Hyperthyroidism	8	(5.4)	0		76	(5.7)	2	(0.2)
Severe skin reactions	4	(2.7)	3	(2.0)	30	(2.3)	24	(1.8)
Hypophysitis	3	(2.0)	3	(2.0)	5	(0.4)	4	(0.3)
Hepatitis	2	(1.3)	2	(1.3)	10	(0.8)	6	(0.5)
Colitis	2	(1.3)	1	(0.7)	14	(1.1)	9	(0.7)
Adrenal insufficiency	2	(1.3)	1	(0.7)	8	(0.6)	2	(0.2)
Myocarditis	1	(0.7)	1	(0.7)	0		0	
Infusion reactions	1	(0.7)	0		16	(1.2)	1	(0.1)
Thyroiditis	1	(0.7)	0		19	(1.4)	0	
Pancreatitis	1	(0.7)	0		6	(0.5)	4	(0.3)
Myositis	0		0		6	(0.5)	0	
Nephritis	0		0		5	(0.4)	3	(0.2)
Type 1 diabetes mellitus	0		0		4	(0.3)	4	(0.3)

Profil tolérance superposable sujets jeunes

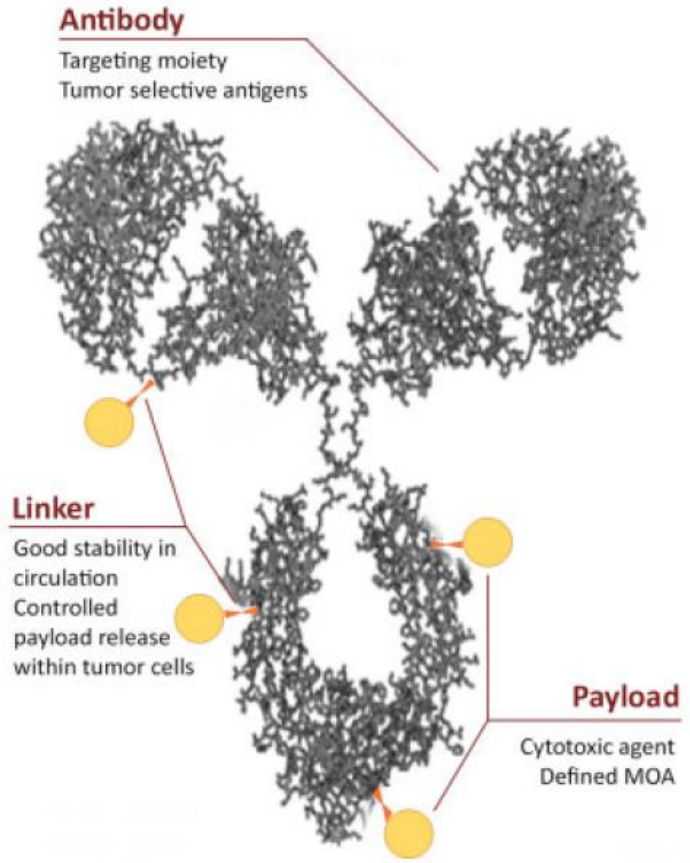
Nosaki et al. Lung cancer; 2019; 135:188-195

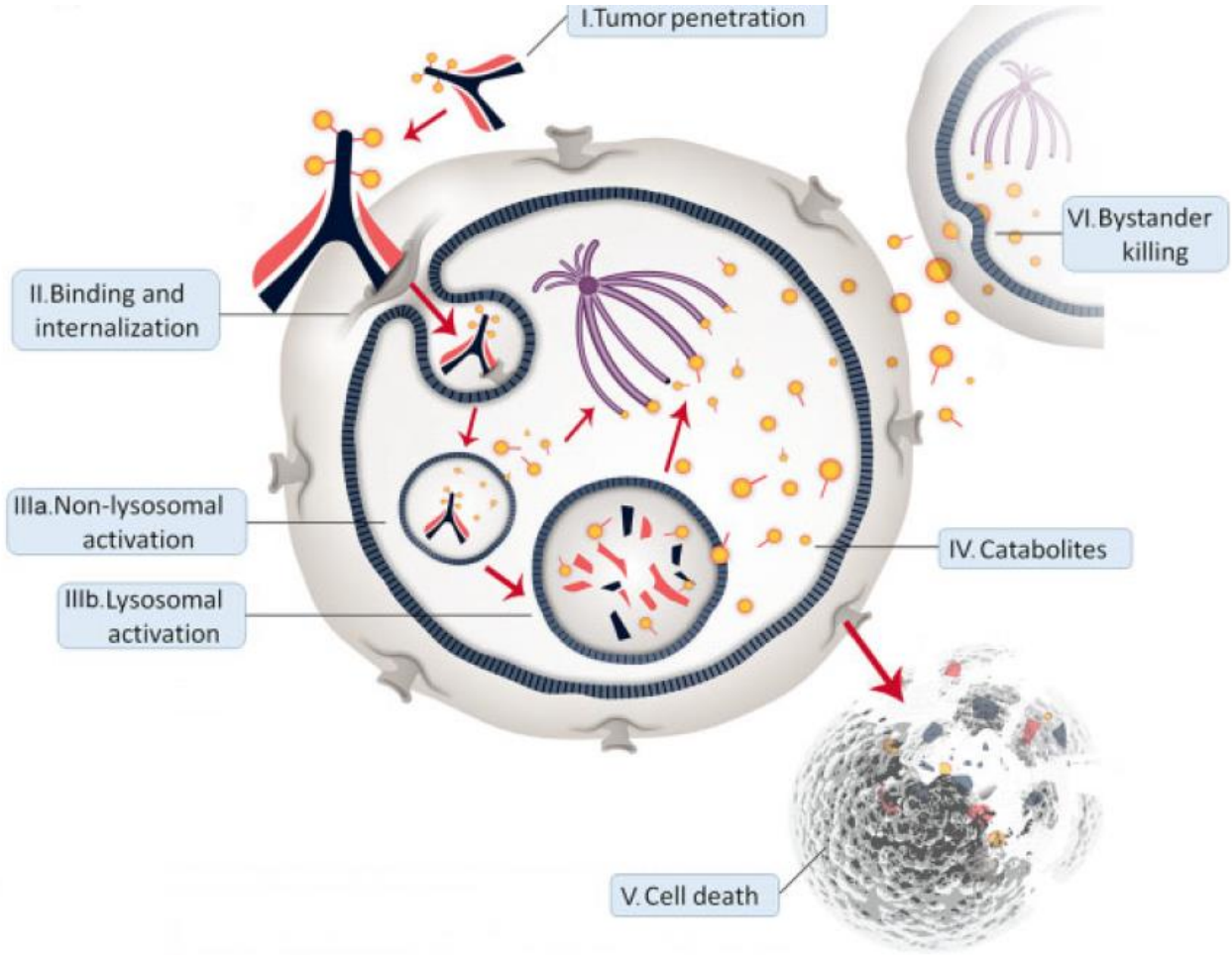
SACITUZUMAB GOVITECAN
TRODELVY®

Mécanisme d'action

Antibody-drug conjugates

Ac monoclonal reconnaissant Ag tumoral + agent cytotoxique par liaison chimique
→ diminue exposition tissus normaux → moins toxicité

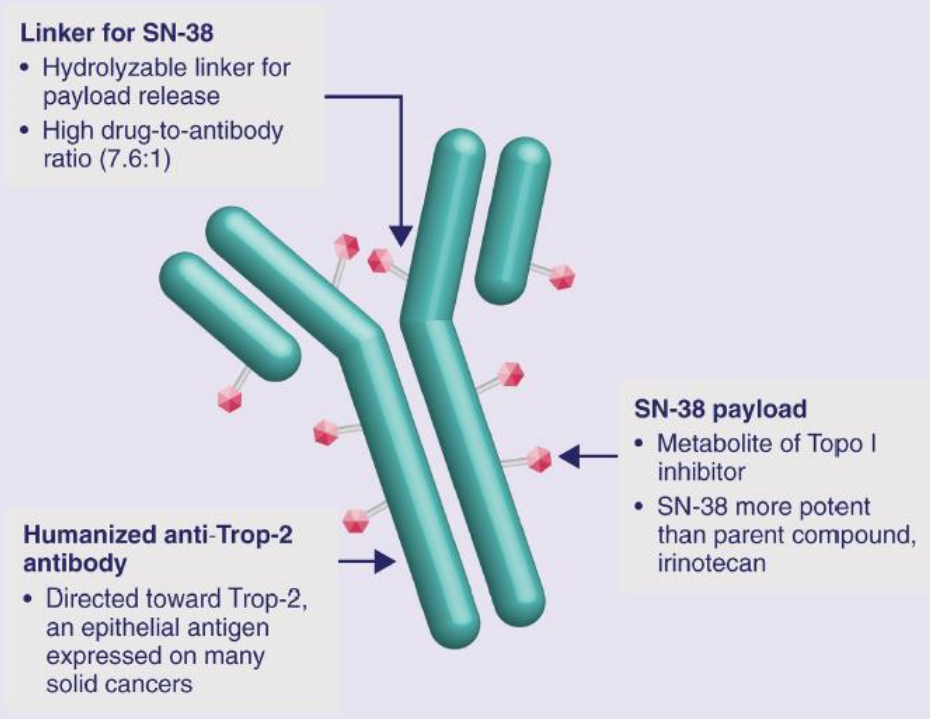


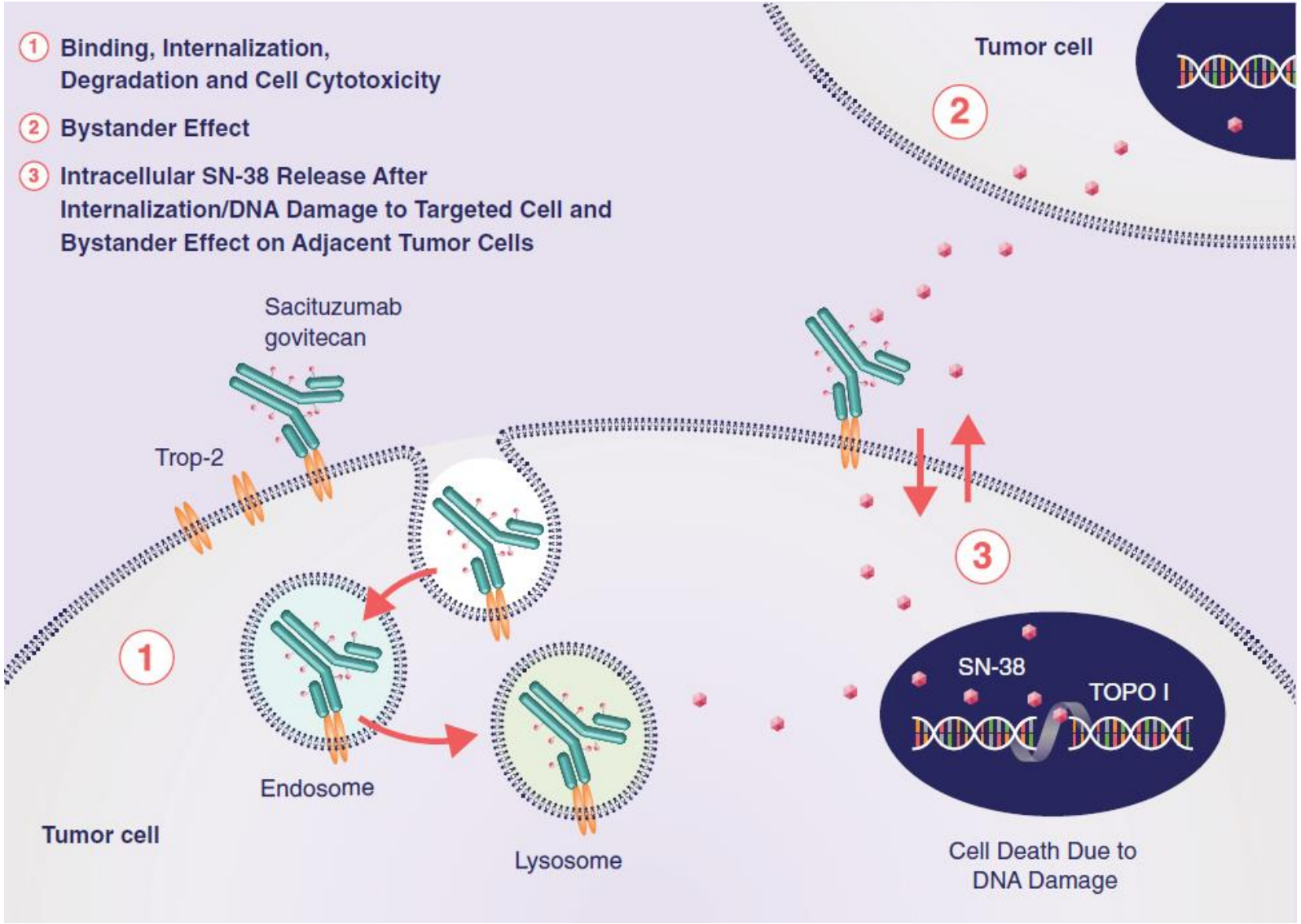


Birrer et al. J Natl Cancer Inst; 2019; 111(6): djz035

Mécanisme d'action

Sacituzumab govitecan - Trodelvy®





Trop 2

Exprimé > 90% cancer sein

Mauvais pronostic

SN38

Métabolite actif Irinotecan

Membrane perméable

Rugo et al. Future Oncol 202; 16(12), 705-715

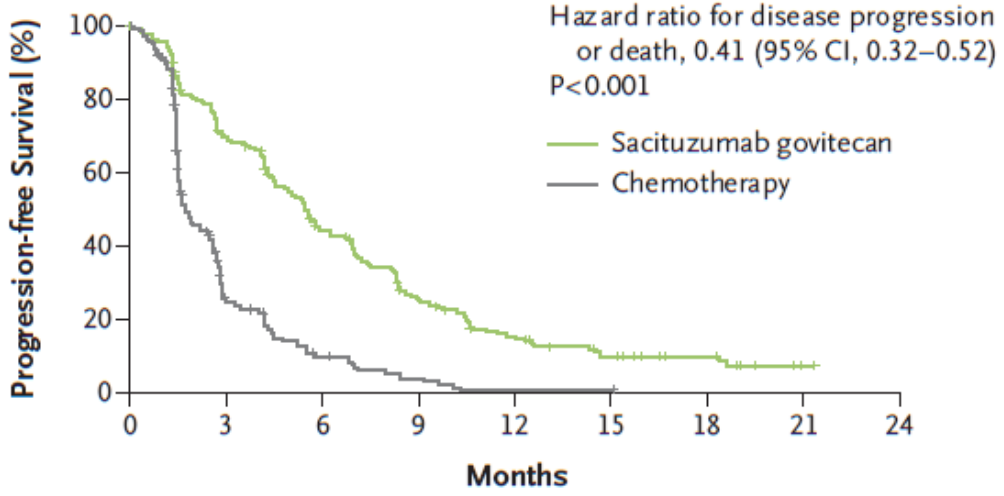
Efficacité

ASCENT

Métastatique TBNC > L2

A Progression-free Survival among Patients without Brain Metastases

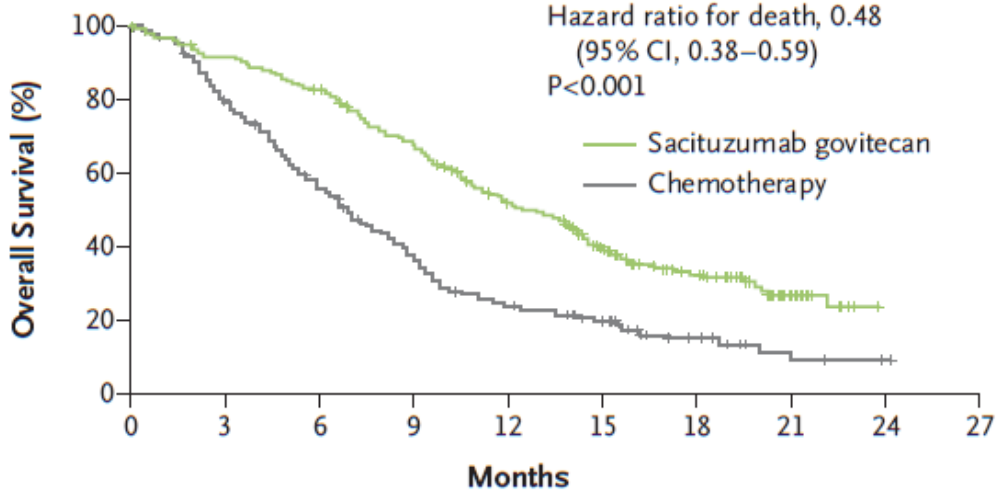
	No. of Patients	No. of Events	Median Progression-free Survival *mo (95% CI)*
Sacituzumab Govitecan	235	166	5.6 (4.3–6.3)
Chemotherapy	233	150	1.7 (1.5–2.6)



No. at Risk								
Sacituzumab govitecan	235	154	91	49	28	15	9	1
Chemotherapy	233	39	14	5	1	1	0	0

B Overall Survival among Patients without Brain Metastases

	No. of Patients	No. of Events	Median Overall Survival *mo (95% CI)*
Sacituzumab Govitecan	235	155	12.1 (10.7–14.0)
Chemotherapy	233	185	6.7 (5.8–7.7)



No. at Risk									
Sacituzumab govitecan	235	214	190	153	107	70	37	13	0
Chemotherapy	233	173	117	74	45	30	11	3	1

Bardia et al. N Engl J Med; 2021; 384:1529-41

Tolérance

Adverse Event	Sacituzumab Govitecan (N=258)			Chemotherapy (N=224)		
	Any Grade	Grade 3	Grade 4	Any Grade	Grade 3	Grade 4
	number of patients (percent)					
Any adverse event	252 (98)	117 (45)	48 (19)	192 (86)	71 (32)	33 (15)
Hematologic event						
Neutropenia†	163 (63)	88 (34)	44 (17)	96 (43)	45 (20)	29 (13)
Anemia‡	89 (34)	20 (8)	0	54 (24)	11 (5)	0
Leukopenia§	41 (16)	23 (9)	3 (1)	25 (11)	10 (4)	2 (1)
Thrombocytopenia¶	14 (5)	2 (1)	2 (1)	25 (11)	3 (1)	0
Febrile neutropenia	15 (6)	12 (5)	3 (1)	5 (2)	4 (2)	1 (<1)
Gastrointestinal event						
Diarrhea	153 (59)	27 (10)	0	27 (12)	1 (<1)	0
Nausea	147 (57)	6 (2)	1 (<1)	59 (26)	1 (<1)	0
Vomiting	75 (29)	2 (1)	1 (<1)	23 (10)	1 (<1)	0
Constipation	44 (17)	0	0	32 (14)	0	0
Abdominal pain	29 (11)	3 (1)	0	9 (4)	1 (<1)	0
General disorders and administration-site conditions						
Fatigue	115 (45)	8 (3)	0	68 (30)	12 (5)	0
Asthenia	31 (12)	2 (1)	0	23 (10)	3 (1)	0
Skin and subcutaneous disorders: alopecia‖	119 (46)	0	0	35 (16)	0	0
Metabolism and nutrition disorders: decreased appetite	51 (20)	4 (2)	0	32 (14)	1 (<1)	0
Nervous system disorders**††	64 (25)	1 (<1)	0	53 (24)	5 (2)	0
Respiratory, thoracic, and mediastinal disorders††	41 (16)	5 (2)‡‡	0	17 (8)	1 (<1)	0
Musculoskeletal and connective-tissue disorders††	32 (12)	0	0	28 (12)	3 (1)	0
Infections and infestations††	30 (12)	6 (2)	1 (<1)	22 (10)	4 (2)	3 (1)

Bardia et al. N Engl J Med; 2021; 384:1529-41

Table 2. Selected key TRAEs of interest observed in ≥20% of patients in the overall safety population (*N* = 495)

TRAE, *n* (%)	All grades	Grade 3	Grade 4
Any adverse reaction, *n* (%)	483 (97.6)	284 (57.4)	73 (14.7)
Gastrointestinal			
Nausea	310 (62.6)	18 (3.6)	0
Diarrhea	278 (56.2)	39 (7.9)	0
Vomiting	191 (38.6)	14 (2.8)	0
Hematologic			
Neutropenia	286 (57.8)	143 (28.9)	67 (13.5)
Febrile neutropenia[a]	27 (5.5)	21 (4.2)	5 (1.0)
Anemia	173 (34.9)	51 (10.3)	0
Systemic/other			
Fatigue	239 (48.3)	31 (6.3)	0
Alopecia	200 (40.4)	0	0

Bardia et al Annals of Oncol; 2021; vol 32 issue 6

Tolérance

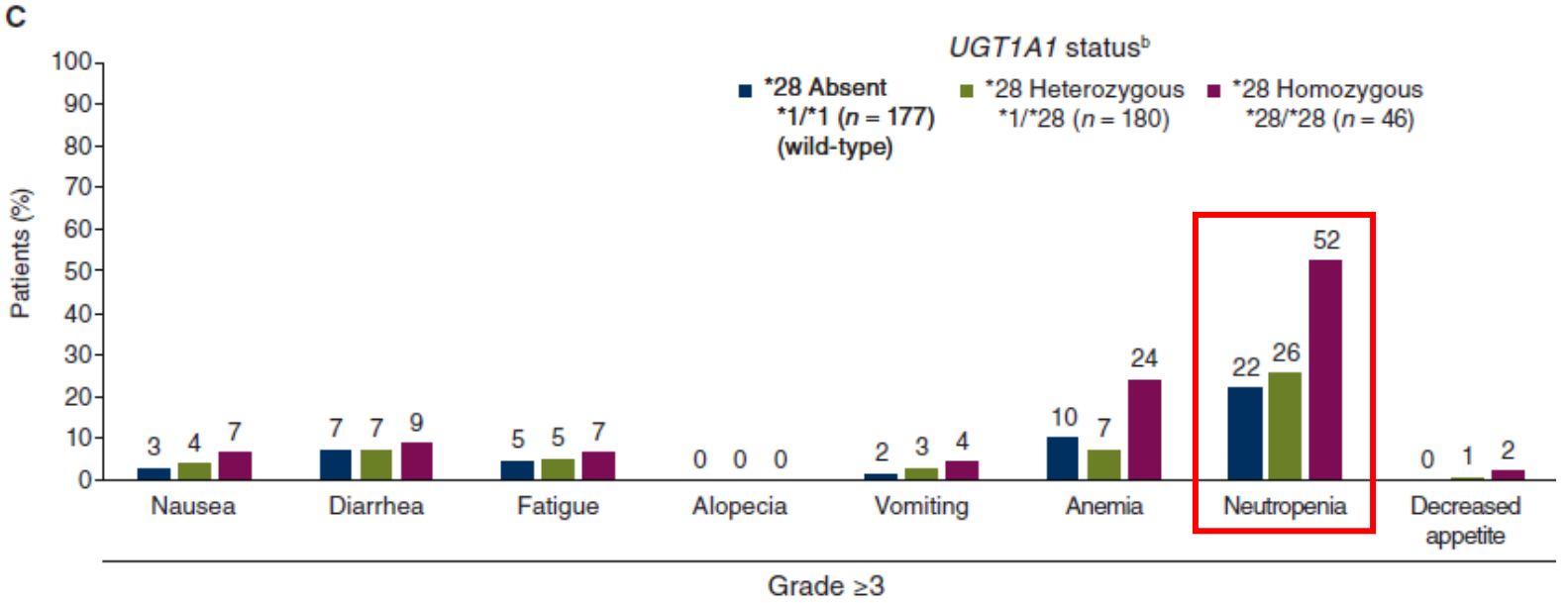


Table 5. TRAEs by *UGT1A1* Genotype (All Grade, >20%; Grade 3/4, >5% of Patients)

		SG (n=250)[†]					
		*1/*1 Wild-Type (n=113)		*1/*28 Heterozygous (n=96)		*28/*28 Homozygous (n=34)	
	TRAE[‡]	All Grade, %	Grade ≥3, %	All Grade, %	Grade ≥3, %	All Grade, %	Grade ≥3, %
Hematologic	**Neutropenia[§]**	**76 (67)**	**60 (53)**	**55 (57)**	**45 (47)**	**24 (71)**	**20 (59)**
	Anemia[‖]	37 (33)	5 (4)	29 (30)	6 (6)	16 (47)	5 (15)
	Leukopenia**	18 (16)	10 (9)	13 (14)	9 (9)	8 (24)	5 (15)
	Lymphopenia[¶]	10 (9)	1 (1)	5 (5)	1 (1)	4 (12)	2 (6)
	Febrile neutropenia	**3 (3)**	**3 (3)**	**5 (5)**	**5 (5)**	**6 (18)**	**6 (18)**
	Thrombocytopenia[=]	3 (3)	0	6 (6)	0	4 (12)	4 (12)
Gastrointestinal	**Diarrhea**	**65 (58)**	**11 (10)**	**57 (59)**	**9 (9)**	**21 (62)**	**5 (15)**

Bardia et al Annals of Oncol; 2021; vol 32 issue 6
Rubo et al. San Antonio Breast Cancer Symposium; 2020; poster PS11-09

Indications

HAUTE AUTORITÉ DE SANTÉ

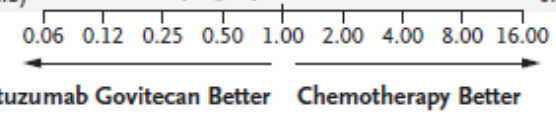
AMM

TRODELVY (sacituzumab govitecan) est un traitement des patients adultes atteints de cancer du sein triple négatif (TNBC) non résécable ou métastatique ayant déjà reçu au moins deux traitements systémiques, dont au moins un pour une forme avancée de la maladie.

En prenant en compte l'introduction récente dans la stratégie thérapeutique de l'immunothérapie (pembrolizumab) en première ligne du cancer du sein triple négatif, la place du sacituzumab govitecan en cas de tumeur avec expression du PD-L1, reste à définir.

Données chez les personnes âgées

Subgroup	No. of Patients	Progression-free Survival		Hazard Ratio for Disease Progression or Death (95% CI)
		Sacituzumab govitecan	Chemotherapy	
		mo (95% CI)		
All patients	468	5.6 (4.3–6.3)	1.7 (1.5–2.6)	0.41 (0.32–0.52)
Age				
<65 yr	378	4.6 (3.7–5.7)	1.7 (1.5–2.5)	0.46 (0.35–0.59)
≥65 yr	90	7.1 (5.8–8.9)	2.4 (1.4–2.9)	0.22 (0.12–0.40)
Race				
White	369	5.7 (4.3–6.8)	1.7 (1.5–2.6)	0.39 (0.30–0.51)
Black	56	5.4 (2.8–7.4)	2.2 (1.5–2.9)	0.45 (0.24–0.86)
Asian	18	NE (1.3–NE)	1.5 (1.2–NE)	0.40 (0.08–2.08)
Previous therapies				
2 or 3	330	5.8 (4.2–7.1)	1.6 (1.5–2.5)	0.39 (0.29–0.52)
>3	138	5.6 (3.0–6.5)	2.5 (1.5–2.8)	0.48 (0.32–0.72)
Geographic region				
North America	298	4.9 (4.0–6.3)	2.0 (1.5–2.6)	0.44 (0.33–0.60)
Rest of the world	170	5.9 (4.2–6.9)	1.6 (1.4–2.7)	0.36 (0.24–0.53)
Previous use of PD-1 or PD-L1 inhibitors				
Yes	127	4.2 (3.2–5.6)	1.6 (1.4–2.3)	0.37 (0.24–0.57)
No	341	6.2 (4.9–7.1)	2.1 (1.5–2.7)	0.42 (0.32–0.56)
Liver metastasis				
Yes	199	4.2 (2.8–5.8)	1.5 (1.4–2.4)	0.48 (0.34–0.67)
No	269	6.8 (4.6–8.0)	2.3 (1.6–2.7)	0.36 (0.26–0.50)
Initial diagnosis of TNBC				
Yes	322	5.7 (4.3–6.9)	1.6 (1.5–2.6)	0.38 (0.29–0.51)
No	146	4.6 (3.7–6.9)	2.3 (1.5–2.8)	0.48 (0.32–0.72)



	SG	Chimiothérapie
≥ 65 ans	49 (19%)	48 (21%)
≥ 75 ans	8 (3%)	13 (5,8%)

Bardia et al. N Engl J Med; 2021; 384:1529-41

Données chez les personnes âgées

	SG	Chimiothérapie
≥ 65 ans	49 (19%)	48 (21%)
≥ 75 ans	8 (3%)	13 (5,8%)

Table 2. Treatment-related adverse events of all grades reported in >20% and of grade 3 or 4 reported in >5% of patients by age.

TRAE[1], *n (%)*	SG						TPC					
	<65 years (*n* = 209)			≥65 years (*n* = 49)			<65 years (*n* = 176)			≥65 years (*n* = 48)		
	All grades	Grade 3	Grade 4	All grades	Grade 3	Grade 4	All grades	Grade 3	Grade 4	All grades	Grade 3	Grade 4
Hematologic												
Neutropenia[2]	134 (64)	76 (36)	34 (16)	29 (59)	12 (24)	10 (20)	75 (43)	30 (17)	25 (14)	21 (44)	15 (31)	4 (8)
Anemia[3]	63 (30)	13 (6)	0	26 (53)	7 (14)	0	40 (23)	8 (5)	0	14 (29)	3 (6)	0
Leukopenia[4]	33 (16)	19 (9)	2 (1)	8 (16)	4 (8)	1 (2)	18 (10)	8 (5)	2 (1)	7 (15)	2 (4)	0
Febrile neutropenia	11 (5)	10 (5)	1 (<1)	4 (8)	2 (4)	2 (4)	5 (3)	4 (2)	1 (1)	0	0	0
Gastrointestinal												
Diarrhea	121 (58)	22 (11)	0	32 (65)	5 (10)	0	20 (11)	1 (1)	0	7 (15)	0	0
Nausea	123 (59)	6 (3)	1 (<1)	24 (49)	0	0	48 (27)	0	0	11 (23)	1 (2)	0
Constipation	32 (15)	0	0	12 (24)	0	0	27 (15)	0	0	5 (10)	0	0
Vomiting	63 (30)	2 (1)	1 (<1)	12 (24)	0	0	20 (11)	0	0	3 (6)	1 (2)	0
Other												
Fatigue	91 (44)	6 (3)	0	24 (49)	2 (4)	0	49 (28)	10 (6)	0	19 (40)	2 (4)	0
Alopecia	101 (48)	0	0	18 (37)	0	0	27 (15)	0	0	8 (17)	0	0
Decreased appetite	40 (19)	2 (1)	0	11 (22)	2 (4)	0	25 (14)	1 (1)	0	7 (15)	0	0

Profil tolérance idem <65 ans

+ réduction dose ≥ 65ans

- Asthénie
- Nausée
- Diarrhée
- Neutropénie fébrile

Rugo et al. npj Breast Cancer; 2022; 8:98

TRASTUZUMAB EMTANSINE
KADCYLA®

Mécanisme d'action

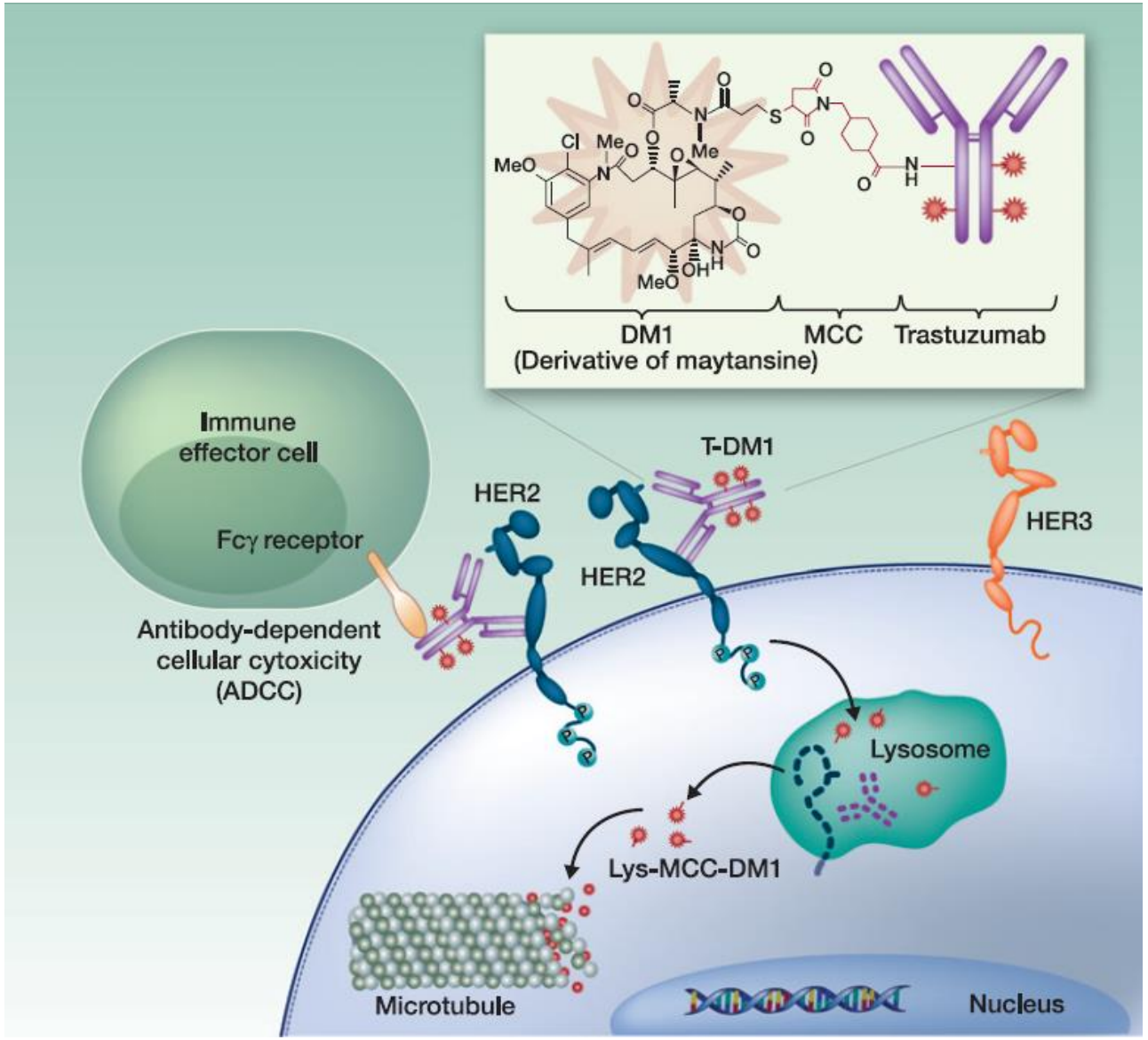
ADC : Trastuzumab Emtansine - Kadcyla®

HER 2

- Surexprimé différents cancers
- 10-20% Cancers sein
- Mauvais pronostic

DM1

- Dérivé maytansine
- Inhibiteur microtubules

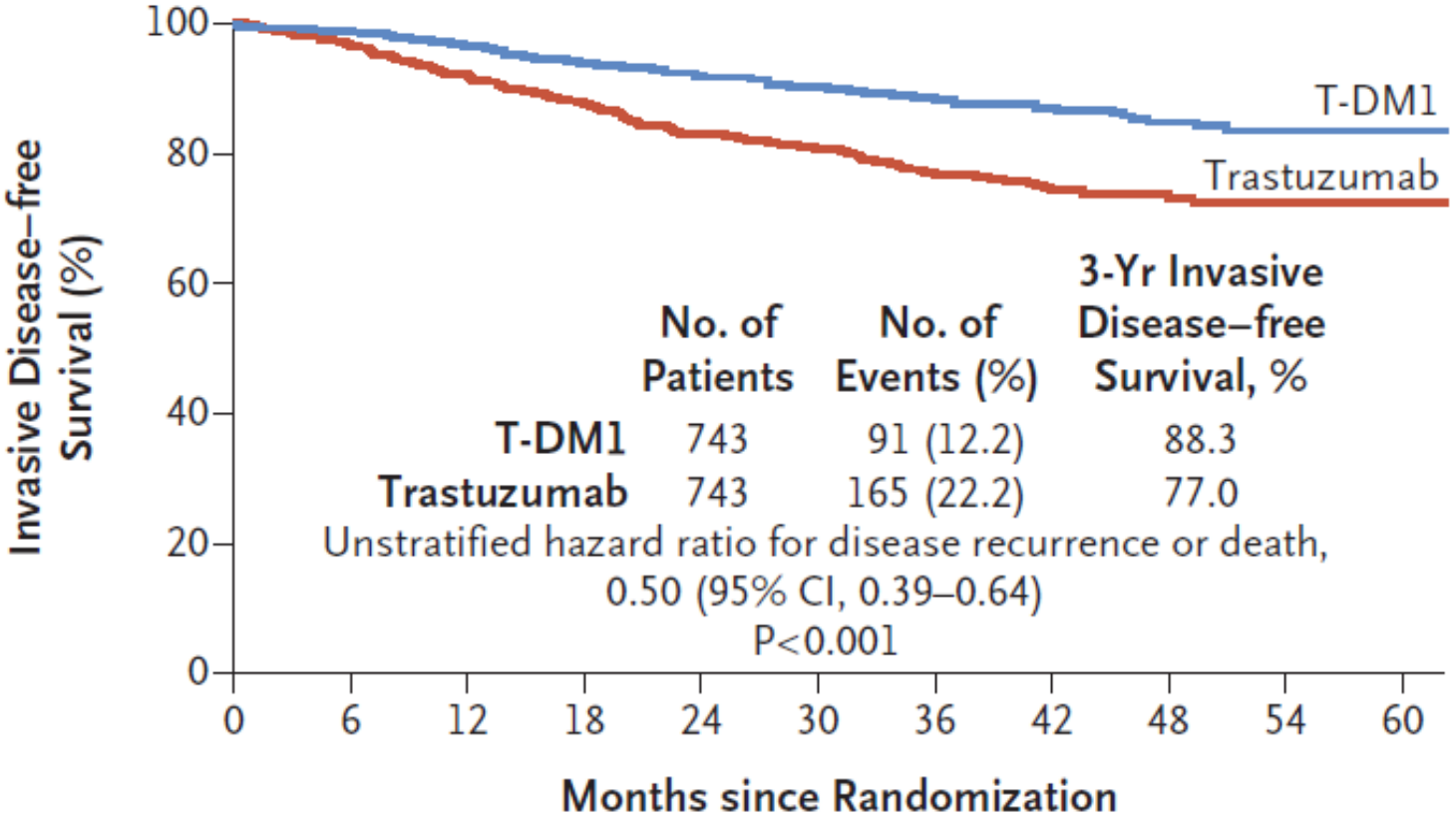


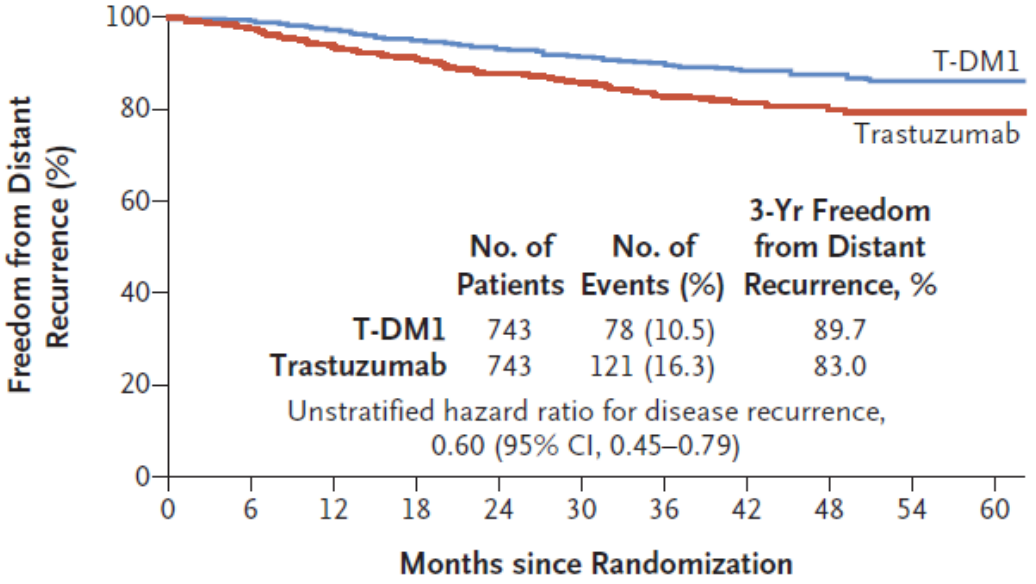
LoRusso et al. Clin Cancer Res; 2011; 17 (20): 6437-47

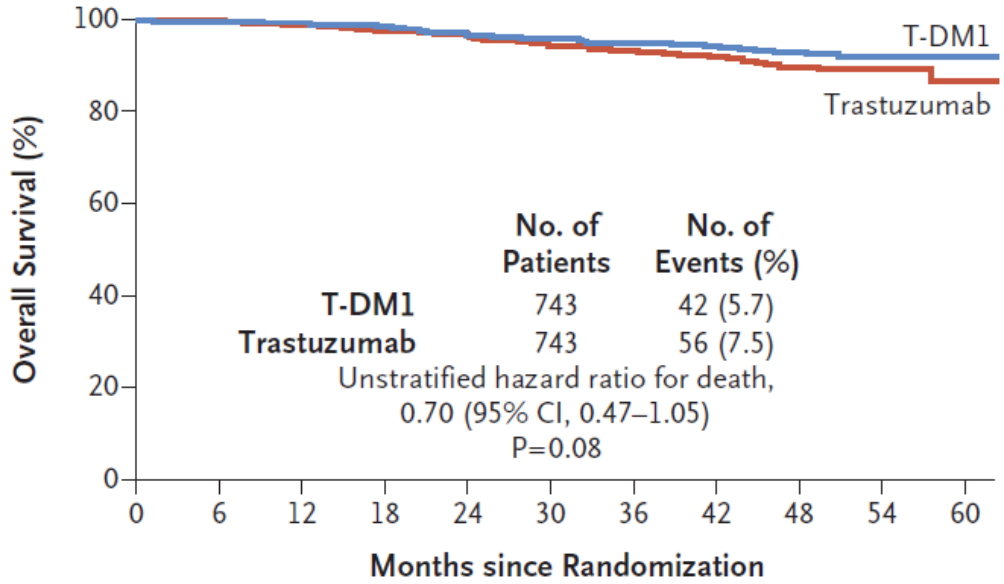
Efficacité

KATHERINE

Cancers seins HER2+ localisés
Mdie résiduelle invasive après chimio néodadj







Minckwitz et al. N Engl J Med; 2019; 380:617-28

Tolérance

Event	Trastuzumab Group (N=720)	T-DM1 Group (N=740)
	no. of patients (%)	
Any adverse event	672 (93.3)	731 (98.8)
Grade ≥3 adverse event	111 (15.4)	190 (25.7)
Adverse event leading to death†	0	1 (0.1)
Serious adverse event	58 (8.1)	94 (12.7)
Adverse event leading to discontinuation of trial drug‡	15 (2.1)	133 (18.0)
Grade ≥3 adverse event that occurred in ≥1% of patients in either group		
Decreased platelet count	2 (0.3)	42 (5.7)
Hypertension	9 (1.2)	15 (2.0)
Radiation-related skin injury	7 (1.0)	10 (1.4)
Peripheral sensory neuropathy	0	10 (1.4)
Decreased neutrophil count	5 (0.7)	9 (1.2)
Hypokalemia	1 (0.1)	9 (1.2)
Fatigue	1 (0.1)	8 (1.1)
Anemia	1 (0.1)	8 (1.1)

Neuropathie périph sensitive = 1,4 % G3
Diminution FEVG = 1,2%

Surveillance FEVG

Minckwitz et al. N Engl J Med; 2019; 380:617-28

Indications

HAUTE AUTORITÉ DE SANTÉ

Extension d'indication

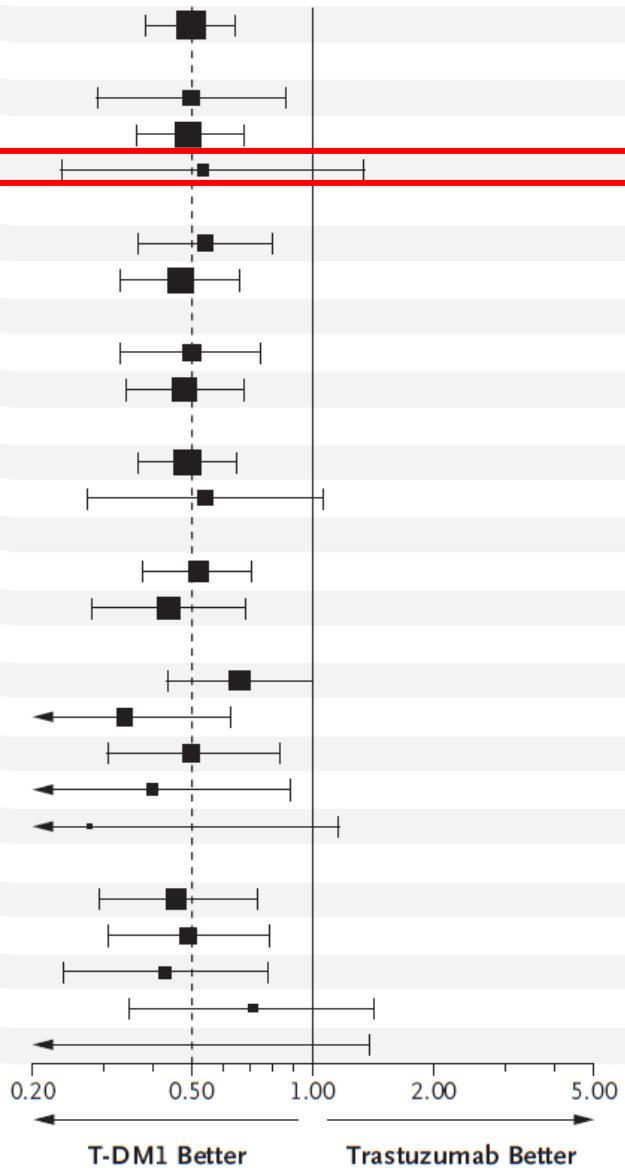
AMM

Nouvelle indication.

Avis favorable au remboursement dans le traitement adjuvant de patients adultes atteints d'un cancer du sein précoce HER2 positif qui ont une maladie résiduelle invasive, au niveau du sein et/ou des ganglions lymphatiques, après un traitement néoadjuvant à base de taxane et d'un traitement anti-HER2.

Données chez les personnes âgées

Subgroup	T-DM1 (no. of patients with an invasive-disease event/total no.)	Trastuzumab (no. of patients with an invasive-disease event/total no.)	Hazard Ratio for Invasive-Disease Event (95% CI)	3-Yr Invasive Disease–free Survival Rate: T-DM1 (%)	3-Yr Invasive Disease–free Survival Rate: Trastuzumab (%)
All patients	91/743	165/743	0.50 (0.39–0.64)	88.3	77.0
Age group					
<40 yr	20/143	37/153	0.50 (0.29–0.86)	86.5	74.9
40–64 yr	64/542	113/522	0.49 (0.36–0.67)	88.8	77.1
≥65 yr	7/58	15/68	0.55 (0.22–1.34)	87.4	81.1
Clinical stage at presentation					
Inoperable breast cancer	42/185	70/190	0.54 (0.37–0.80)	76.0	60.2
Operable breast cancer	49/558	95/553	0.47 (0.33–0.66)	92.3	82.8
Hormone-receptor status					
Negative (ER-negative and progesterone-receptor–negative or unknown)	38/209	61/203	0.50 (0.33–0.74)	82.1	66.6
Positive (ER-positive, progesterone-receptor–positive, or both)	53/534	104/540	0.48 (0.35–0.67)	90.7	80.7
Preoperative HER2-directed therapy					
Trastuzumab alone	78/600	141/596	0.49 (0.37–0.65)	87.7	75.9
Trastuzumab plus additional HER2-directed agent or agents	13/143	24/147	0.54 (0.27–1.06)	90.9	81.8
Pathological nodal status after preoperative therapy					
Node-positive	62/343	103/346	0.52 (0.38–0.71)	83.0	67.7
Node-negative or NE	29/400	62/397	0.44 (0.28–0.68)	92.8	84.6
Primary tumor stage at definitive surgery					
ypT0, ypT1a, ypT1b, ypT1mic, ypTis	40/331	52/306	0.66 (0.44–1.00)	88.3	83.6
ypT1, ypT1c	14/175	42/184	0.34 (0.19–0.62)	91.9	75.9
ypT2	25/174	44/185	0.50 (0.31–0.82)	88.3	74.3
ypT3	9/51	21/57	0.40 (0.18–0.88)	79.8	61.1
ypT4	3/12	6/11	0.29 (0.07–1.17)	70.0	30.0
Regional lymph-node stage at definitive surgery					
ypN0	28/344	56/335	0.46 (0.30–0.73)	91.9	83.9
ypN1	29/220	50/213	0.49 (0.31–0.78)	88.9	75.8
ypN2	16/86	38/103	0.43 (0.24–0.77)	81.1	58.2
ypN3	17/37	15/30	0.71 (0.35–1.42)	52.0	40.6
ypNX	1/56	6/62	0.17 (0.02–1.38)	98.1	88.7



Minckwitz et al. N Engl J Med; 2019; 380:617-28

Données chez les personnes âgées

Outcome, n (%)	≥ 65 yrs (n = 373)	< 65 yrs (n = 1628)
Discontinuation due to AEs (% based on pts who discontinued)	41 (14.3)	112 (9.5)
Fatal AEs	10 (2.7)	17 (1.0)
Grade ≥ 3 AEs	160 (42.9)	540 (33.2)
Grade ≥ 3 AEs in ≥ 2% of either group		
Thrombocytopenia*	13 (3.5)	53 (3.3)
Asthenia	12 (3.2)	18 (1.1)
Anemia	11 (2.9)	32 (2.0)
Fatigue	10 (2.7)	34 (2.1)
GGT increased	8 (2.1)	42 (2.6)
Thrombocytopenia* Grade ≥ 3	49 (13.1) 13 (3.5)	211 (13.0) 53 (3.3)
Hepatotoxicity* Grade ≥ 3	68 (18.2) 18 (4.8)	327 (20.1) 114 (7.0)
Hemorrhage* Grade ≥ 3	87 (23.3) 6 (1.6)	392 (24.1) 28 (1.7)
LVEF < 45%	5 (1.3)**	36 (2.2)

*Based on groupings of related preferred terms; **None < 40%.

Analyse sous groupe étude Kamilla

Barrios et al. J Clin Oncol; 2015; 33(15):603

Données chez les personnes âgées

Characteristics	Median (range) or n (%)
Age, y	71 (65–89)
65–74	24 (25.8)
⩾75	69 (74.2)
ECOG Performance Status	
0	25 (26.9)
1	40 (43)
2	28 (30.1)
Disease extent at diagnosis	
Early	73 (78.5)
Metastatic	20 (21.5)
Histologic subtype	
Invasive ductal carcinoma	82 (88.2)
Other	11 (11.8)
Hormone receptor status	
ER+ or PR+	55 (59.2)
ER– and PR–	38 (40.8)
Visceral metastases	
Yes	65 (69.9)
No	28 (30.1)
CNS metastasis	
Yes	32 (34.4)
No	61 (65.6)
Number of metastatic sites	
>3	52 (55.9)
<3	41 (44.1)
T-DM1 treatment line	
First	21 (22.6)
Second	42 (45.2)
Third	21 (22.6)
Fourth or more	9 (9.7)

AEs	Events of any grade, n (%)	Events of grade 3 or above, n (%)
Any event	86 (92.5)	28 (30.1)
Fatigue	54 (58.1)	5 (5.4)
Nausea	41 (44.1)	1 (1)
Vomiting	23 (24.7)	0 (0)
Diarrhea	23 (24.7)	3 (3.2)
Mucositis	10 (10.8)	1 (1.1)
Neuropathy	12 (12.9)	0 (0)
Rash	3 (3.2)	0 (0)
Epistaxis	9 (9.7)	0 (0)
Decreased LVEF	5 (5.4)	1 (1.1)
Infusion reaction	1 (1.1)	0 (0)
Thrombocytopenia	32 (34.4)	13 (13.9)
Anemia	22 (23.7)	5 (5.4)
Neutropenia	9 (9.7)	2 (2.2)
Elevated AST	27 (29)	3 (3.2)
Elevated ALT	22 (23.7)	3 (3.2)
AEs leading to dose reduction	11 (11.8)	
AEs leading to drug discontinuation	6 (6.5)	

Supérieur à KATHERINE
mais situation M+

Idem KATHERINE
18% diminution dose/arrêt
1,2% diminution FEVG

Cil et al. Tumori journal; 2022;108: 19-25

Données chez les personnes âgées

Des réponses à venir?

Study Design

Study Type :	Interventional (Clinical Trial)
Actual Enrollment :	82 participants
Allocation:	N/A
Intervention Model:	Single Group Assignment
Masking:	None (Open Label)
Primary Purpose:	Treatment
Official Title:	ATOP TRIAL: Adjuvant Ado-Trastuzumab Emtansine (T-DM1) for Older Patients With Human Epidermal Growth Factor Receptor 2 (HER2)-Positive Breast Cancer
Actual Study Start Date :	August 22, 2018
Estimated Primary Completion Date :	August 30, 2026
Estimated Study Completion Date :	August 30, 2029

TRASTUZUMAB DERUXTECAN
ENHERTU®

Mécanisme d'action

ADC : Trastuzumab Deruxtecan - Enhertu®

HER 2

Surexprimé différents cancers

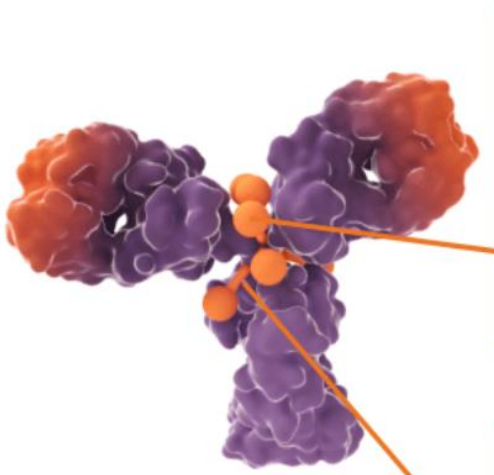
10-20% Cancers sein

DXd

Analogue Captothecin - Inhib topo I

8 molécules/ Ac

Membrane perméable



HER2-directed mAb[1]

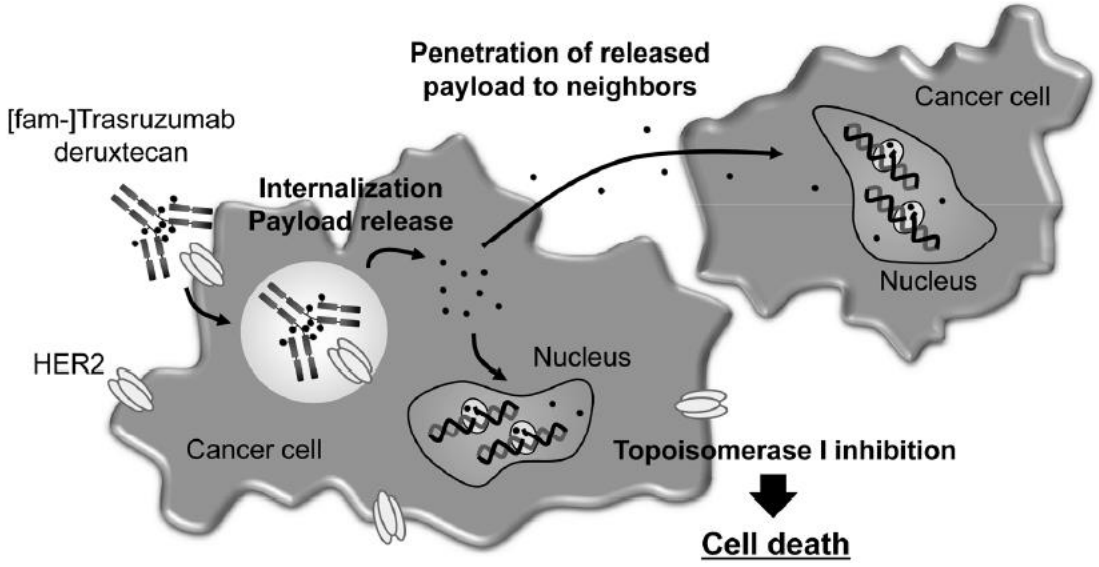
- Provides targeted delivery of cytotoxic agent[1,2]
- Consists of the same amino acid sequence as trastuzumab[3]

Topoisomerase I inhibitor payload[1,2,a]

- Highly potent payload is an exatecan derivative, known as DXd, with a short systemic half-life[1,3]
- Upon release, membrane-permeable payload causes DNA damage and cell death, resulting in destruction of targeted tumor cells and surrounding cells, known as the bystander antitumor effect[1,3,4]

Tumor-selective cleavable linker[1-3,a]

- Attaches payload to the antibody[1]
- Linker-payload is stable in plasma[2,3]
- Linker selectively cleaved by enzymes that are upregulated in tumor cells[1,3]



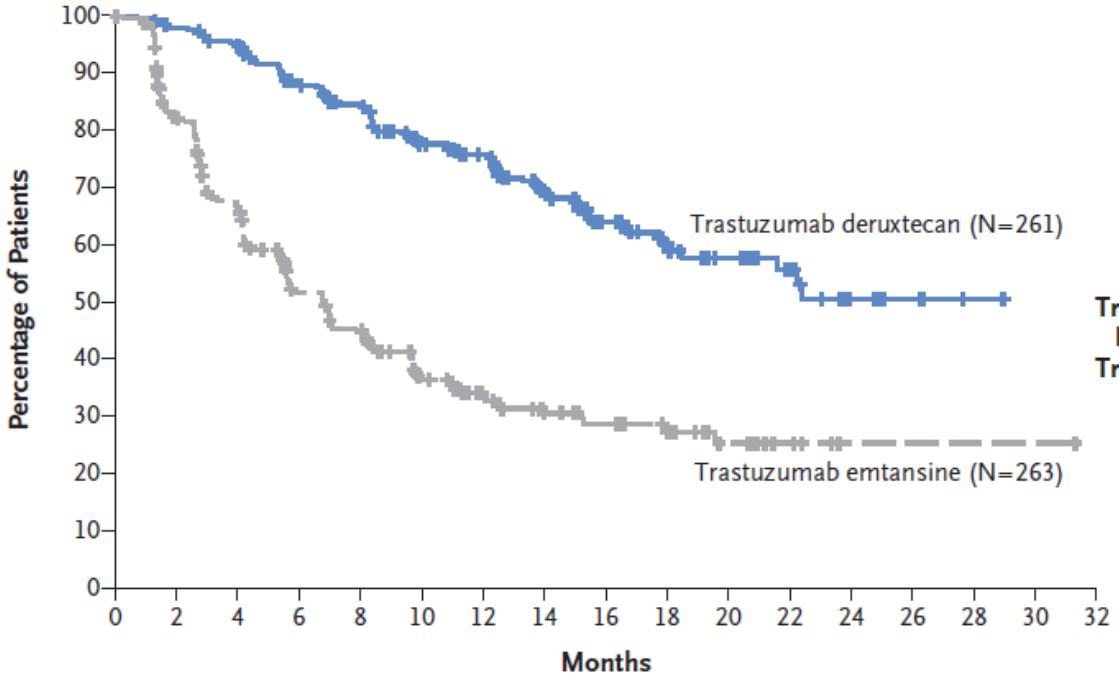
https://www.enhertuhcp.com

Nakada et al. Chem Pharm Bull; 2019; 67: 173-185

Efficacité

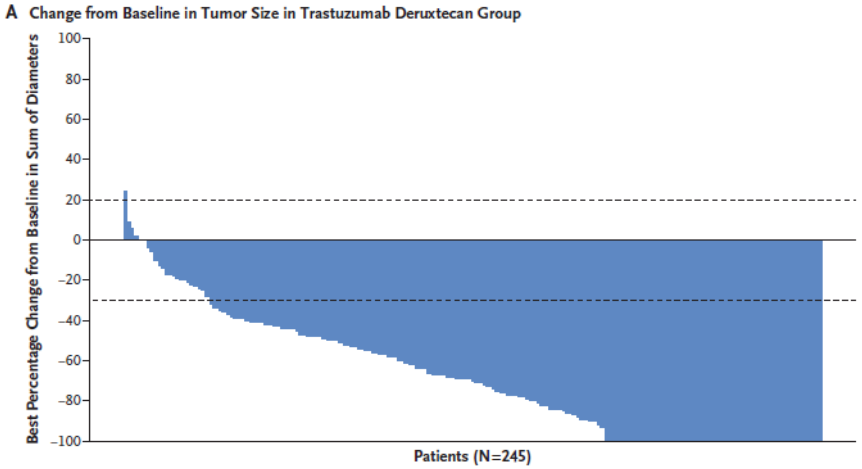
DESTINY-Breast03

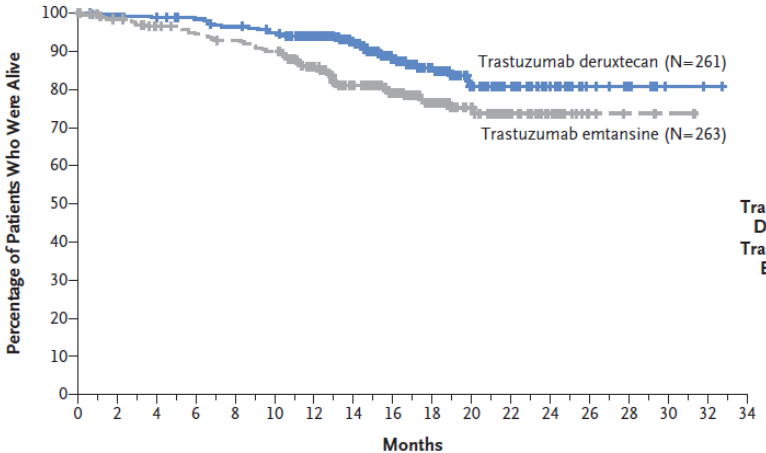
Cancers seins HER2+ > L1 M+
Ou progression ≤6mois TTT forme localisée



	Median Progression-free Survival (95% CI)	12-Mo Progression-free Survival (95% CI)
	mo	%
Trastuzumab Deruxtecan	NR (18.5–NE)	75.8 (69.8–80.7)
Trastuzumab Emtansine	6.8 (5.6–8.2)	34.1 (27.7–40.5)

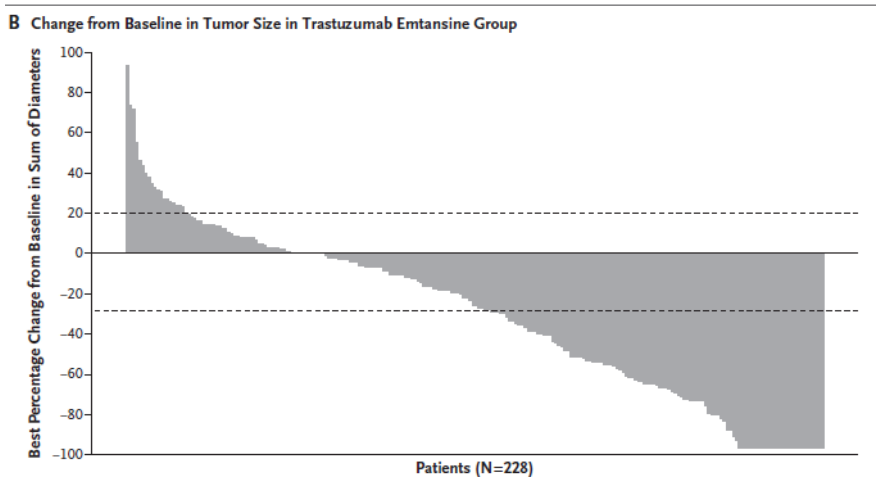
Hazard ratio for disease progression or death, 0.28 (95% CI, 0.22–0.37)
P<0.001





	Median Overall Survival (95% CI)	12-Mo Overall Survival (95% CI)
	mo	%
Trastuzumab Deruxtecan	NE (NE–NE)	94.1 (90.3–96.4)
Trastuzumab Emtansine	NE (NE–NE)	85.9 (80.9–89.7)

Hazard ratio for death, 0.55 (95% CI, 0.36–0.86)
P=0.007



Mais 1ère analyse intermédiaire…

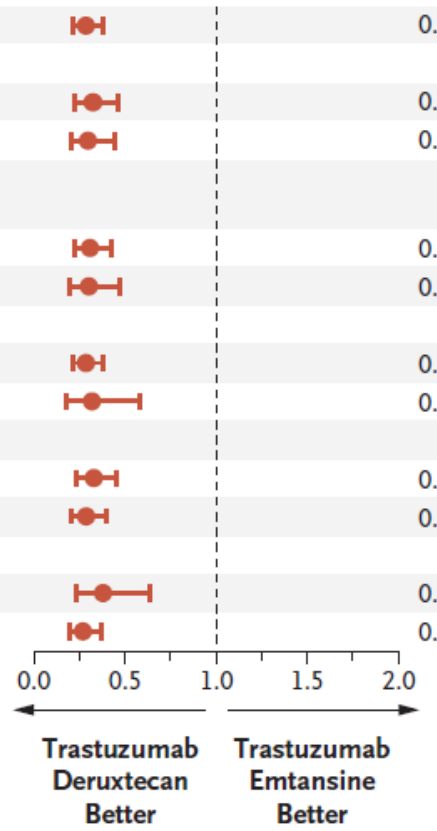
Cortés et al. N Engl J Med; 2022; 386:1143-54

Efficacité

DESTINY-Breast03

Cancers seins HER2+ > L1 M+
Ou progression ≤6mois TTT forme localisée

Subgroup	No. of Patients	No. of Events/No. of Patients		Median Progression-free Survival (95% CI) *mo*		Hazard Ratio for Disease Progression or Death (95% CI)
		Trastuzumab deruxtecan	Trastuzumab emtansine	Trastuzumab deruxtecan	Trastuzumab emtansine	
All patients		87/261	158/263	NE (18.5–NE)	6.8 (5.6–8.2)	0.28 (0.22–0.37)
Hormone-receptor status						
Positive	272	46/133	84/139	22.4 (17.7–NE)	6.9 (4.2–9.8)	0.32 (0.22–0.46)
Negative	248	41/126	73/122	NE (18.0–NE)	6.8 (5.4–8.3)	0.30 (0.20–0.44)
Previous pertuzumab treatment						
Yes	320	57/162	98/158	NE (18.5–NE)	6.8 (5.4–8.3)	0.30 (0.22–0.43)
No	204	30/99	60/105	NE (16.5–NE)	7.0 (4.2–9.7)	0.30 (0.19–0.47)
Visceral disease						
Yes	384	72/195	123/189	22.2 (16.5–NE)	5.7 (4.2–7.0)	0.28 (0.21–0.38)
No	140	15/66	35/74	NE (NE–NE)	11.3 (6.8–NE)	0.32 (0.17–0.58)
Lines of previous therapy						
0 or 1	258	46/132	75/126	22.4 (17.9–NE)	8.0 (5.7–9.7)	0.33 (0.23–0.48)
≥2	266	41/129	83/137	NE (16.8–NE)	5.6 (4.2–7.1)	0.28 (0.19–0.41)
Stable brain metastases						
Yes	114	31/62	31/52	15.0 (12.6–22.2)	5.7 (2.9–7.1)	0.38 (0.23–0.64)
No	410	56/199	127/211	NE (22.4–NE)	7.0 (5.5–9.7)	0.27 (0.19–0.37)



Cortés et al. N Engl J Med; 2022; 386:1143-54

Tolérance

Event	Trastuzumab Deruxtecan (N=257)		Trastuzumab Emtansine (N=261)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
	number of patients (percent)			
Most common drug-related adverse events				
Blood and lymphatic system disorders				
Neutropenia*	110 (42.8)	49 (19.1)	29 (11.1)	8 (3.1)
Anemia†	78 (30.4)	15 (5.8)	37 (14.2)	11 (4.2)
Leukopenia‡	77 (30.0)	17 (6.6)	20 (7.7)	1 (0.4)
Thrombocytopenia§	64 (24.9)	18 (7.0)	135 (51.7)	65 (24.9)
Gastrointestinal disorders				
Nausea	187 (72.8)	17 (6.6)	72 (27.6)	1 (0.4)
Vomiting	113 (44.0)	4 (1.6)	15 (5.7)	1 (0.4)
Diarrhea	61 (23.7)	1 (0.4)	10 (3.8)	1 (0.4)
Constipation	58 (22.6)	0	25 (9.6)	0
General disorders				
Fatigue¶	115 (44.7)	13 (5.1)	77 (29.5)	2 (0.8)
Investigations				
Aspartate aminotransferase increased	60 (23.3)	2 (0.8)	97 (37.2)	13 (5.0)
Alanine aminotransferase increased	50 (19.5)	4 (1.6)	71 (27.2)	12 (4.6)
Metabolism and nutrition disorders				
Decreased appetite	67 (26.1)	3 (1.2)	33 (12.6)	0
Skin and subcutaneous tissue disorders				
Alopecia‖	93 (36.2)	1 (0.4)	6 (2.3)	0
Adjudicated drug-related interstitial lung disease or pneumonitis**	27 (10.5)	2 (0.8)	5 (1.9)	0

Surveillance FEVG
Scanner thorax / 6 semaines

Cortés et al. N Engl J Med; 2022; 386:1143-54

Indications

HAUTE AUTORITÉ DE SANTÉ

ATU

Autorisation d'accès précoce octroyée à la spécialité **ENHERTU (Trastuzumab déruxtécan)** dans l'indication « en monothérapie, dans le traitement de patients adultes atteints d'un cancer du sein HER2-positif non résécable ou métastatique ayant reçu au préalable une ligne de traitement anti- HER2. Les patients doivent :

- avoir reçu un traitement antérieur pour la maladie localement avancée ou métastatique ou
- avoir présenté une progression de la maladie pendant un traitement adjuvant ou dans les six mois suivant sa fin ».

Données chez les personnes âgées

Pas de données spécifique sur les personnes âgées que ce soit dans la DB01 ou dans la DB03…

Efficacité?

Tolérance?

… mais …

Données chez les personnes âgées

	All women			70+			<70		
	HR	95% CI	p	HR	95% CI	p	HR	95% CI	p
Age (reference: < 70) ≥70	1.55	[1.38; 1.73]	<0.01	NA			NA		
Age (continuous variable)	NA			1.05	[1.03; 1.07]	<0.01	1.01	[1.00; 1.01]	0.05
Number of metastatic sites at metastatic diagnosis (reference: 1 site)						<0.01			<0.01
2 sites	1.32	[1.18; 1.49]		1.29	[1.01; 1.65]		1.34	[1.17; 1.53]	
3 sites or more	2.10	[1.85; 2.39]	<0.01	1.87	[1.43; 2.45]		2.17	[1.88; 2.51]	
Visceral metastatic disease (reference: none) (*)			<0.01			<0.01			<0.01
Time-varying effect:									
Estimated HR at 1 year	2.67	[2.10; 3.38]		1.91	[1.21; 3.03]		3.11	[2.33; 4.14]	
Estimated HR at 3 years	3.89	[3.07; 4.94]		2.48	[1.56; 3.92]		4.75	[3.56; 6.32]	
Estimated HR at 5 years	5.68	[4.47; 7.20]		3.20	[2.02; 5.07]		7.24	[5.44; 9.65]	
ER/PgR status (reference: both ER- and PgR-)			<0.01			0.02			<0.01
If no time-varying effect, estimated average HR									
Positive ER or positive PgR	NA	NA		0.77	[0.62; 0.95]		NA		
Undetermined ER/PgR status	NA	NA		1.67	[0.68; 0.95]		NA		
If time-varying effect, estimated HR at 1 year									
Positive ER and/or PgR	0.63	[0.56; 0.71]		NA			0.60	[0.52; 0.68]	
Undetermined ER/PgR status	0.54	[0.32; 0.91]		NA			0.45	[0.24; 0.83]	
If time-varying effect, estimated HR at 3 years									
Positive ER and/or PgR	0.79	[0.71; 0.89]		NA			0.76	[0.67; 0.87]	
Undetermined ER/PgR status	0.68	[0.40; 1.14]		NA			0.57	[0.31; 1.06]	
If time-varying effect, estimated HR at 5 years									
Positive ER and/or PgR	1.00	[0.89; 1.12]		NA			0.97	[0.85; 1.12]	
Undetermined ER/PgR status	0.85	[0.50; 1.43]		NA			0.73	[0.39; 1.36]	
First-line treatment (reference: chemotherapy + anti-HER2 therapy)			0.01			<0.01			
If time-varying effect, estimated HR at 1 year									
Chemotherapy without anti-HER2 therapy (±endocrine therapy)	3.40	[2.86; 4.05]		2.79	[2.05; 3.79]		3.77	[3.04; 4.66]	
Anti-HER2 therapy alone or endocrine therapy alone or both	2.26	[1.80; 2.84]		1.96	[1.43; 2.69]		1.24	[0.78; 1.96]	
If time-varying effect, estimated HR at 3 years									
Chemotherapy without anti-HER2 therapy (±endocrine therapy)	2.00	[1.68; 2.38]		2.04	[1.50; 2.78]		2.11	[1.40; 2.61]	
Anti-HER2 therapy alone or endocrine therapy alone or both	1.33	[1.05; 1.67]		1.44	[1.04; 1.97]		0.69	[0.43; 1.10]	
If time-varying effect, estimated HR at 5 years									<0.01
Chemotherapy without anti-HER2 therapy (±endocrine therapy)	1.17	[0.99; 1.40]		1.49	[1.10; 2.03]		1.18	[0.95; 1.46]	
Anti-HER2 therapy alone or endocrine therapy alone or both	0.78	[0.62; 0.98]		1.05	[0.77; 1.45]		0.39	[0.24; 0.61]	
MFI (months) (reference: < 6 months)						0.05			<0.01
6–24 months	2.58	[2.25; 2.95]		1.42	[1.05; 1.92]		3.06	[2.62; 3.58]	
24 months and more	1.37	[1.24; 1.52]	<0.01	1.01	[0.82; 1.26]		1.52	[1.35; 1.71]	
Center size (number of patients/site) (reference: less than 700 patients)			<0.01						<0.01
700 to 1399 patients	0.87	[0.71; 1.06]		NS			0.91	[0.73; 1.13]	
1400 patients and more	0.63	[0.50; 0.78]		NS			0.63	[0.50; 0.80]	

Absence utilisation thérapie anti-HER2 =

- ↗ risque décès
- ↗ risque progression

  HR = 1,54 IC95 [1,18 - 2,02]

Annonay et al. The Breast; 2021; 60:138-46

Messages clés Cancers du sein

Manque de données dans la population gériatrique sous représentée dans les essais mais…

Triple négatifs

Pembrolizumab

- Néoadj TNBC et L1 M+ TNBC avec CPS ≥ 10
- Efficacité: NS mais effectifs faibles
- Tolérance idem jeunes, EI immunomédiés

Sacituzumab Govitecan

- TNBC M+ > L2
- Efficacité: OUI mais à confirmer?
- Tolérance: profil idem mais + réduction dose
- Homozygote muté UGT1A1 ⚠

HER 2 positifs

Trastuzumab Emtansine – TDM1

- HER2+ maladie invasive résiduelle postNéoadj
- Efficacité: NS mais effectifs faibles
- Tolérance: un peu + toxique mais acceptable
- Surveillance FEVG

Trastuzumab Deruxtecan – TDxD

- HER2+ M+ >L1
- Tolérance et efficacité?
- Surveillance FEVG et TDM thorax lowdose

Merci pour votre attention