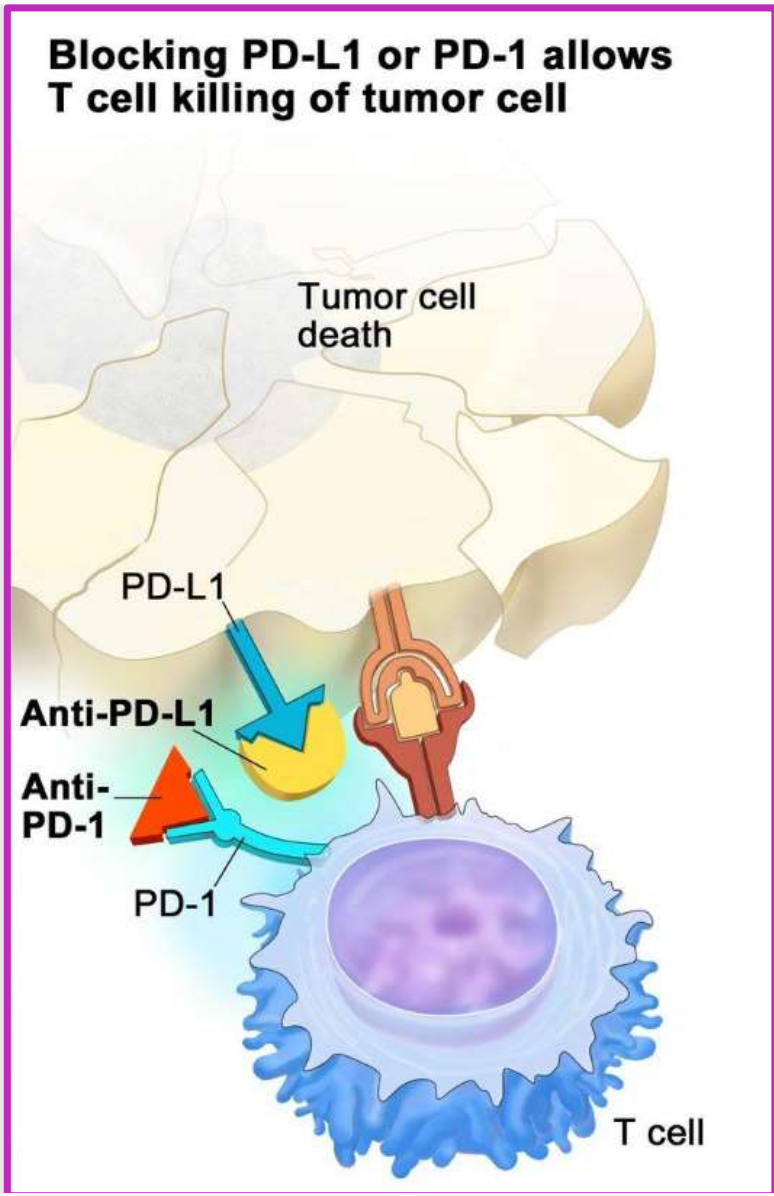
Herbstmeeting der Österreichischen Gesellschaft für Krankenhauspharmazie

(Immun-) onkologische Highlights des Jahres 2024

Dr. Christian Rosker, DAH Oncology

Wien, am 14.10.2023



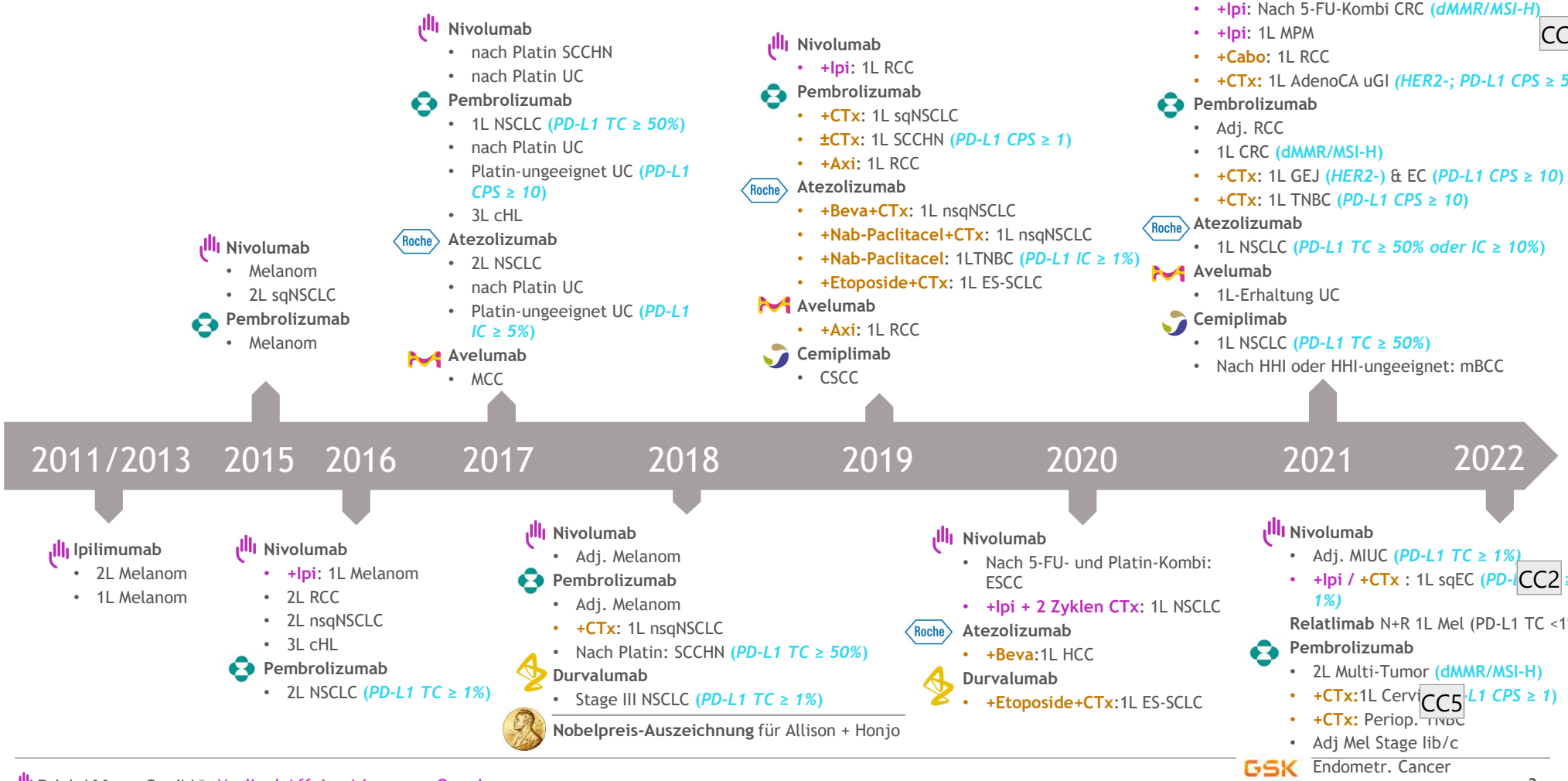
Bristol Myers Squibb™

ONC-AT-2400165

Im Fokus

- Checkpoint Inhibitoren
- EMA Zulassungen
- Positive Ph III Studien
- Kongresse
- Trends

Zulassungsübersicht Immunonkologie



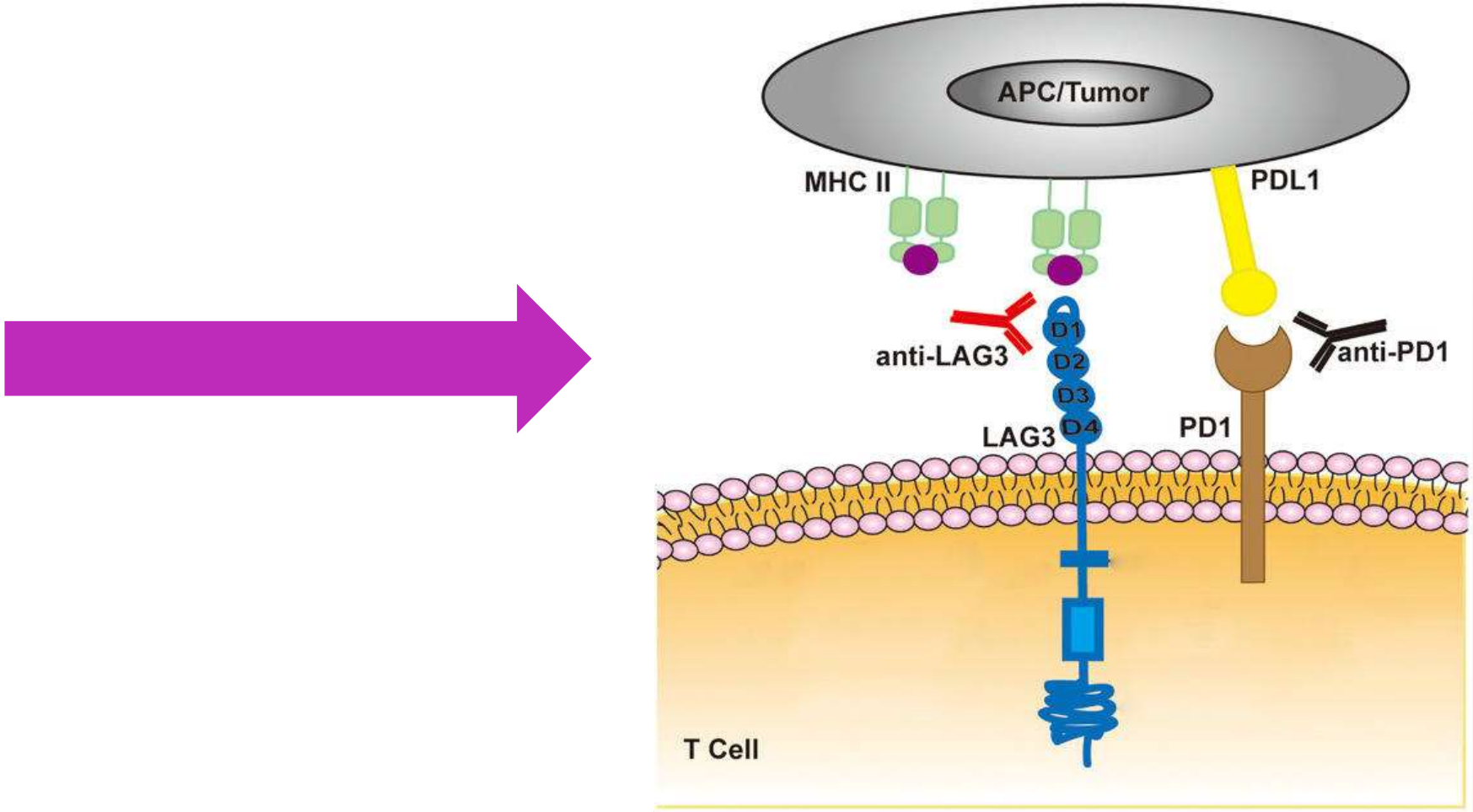
Folie 3

CC1 Hier stand CPS>10, hab es korrigiert.
Campregher, Christoph; 10.10.2022

CC2 Rela eingefügt
Campregher, Christoph; 10.10.2022

CC5 KN-716 eingefügt
Campregher, Christoph; 10.10.2022

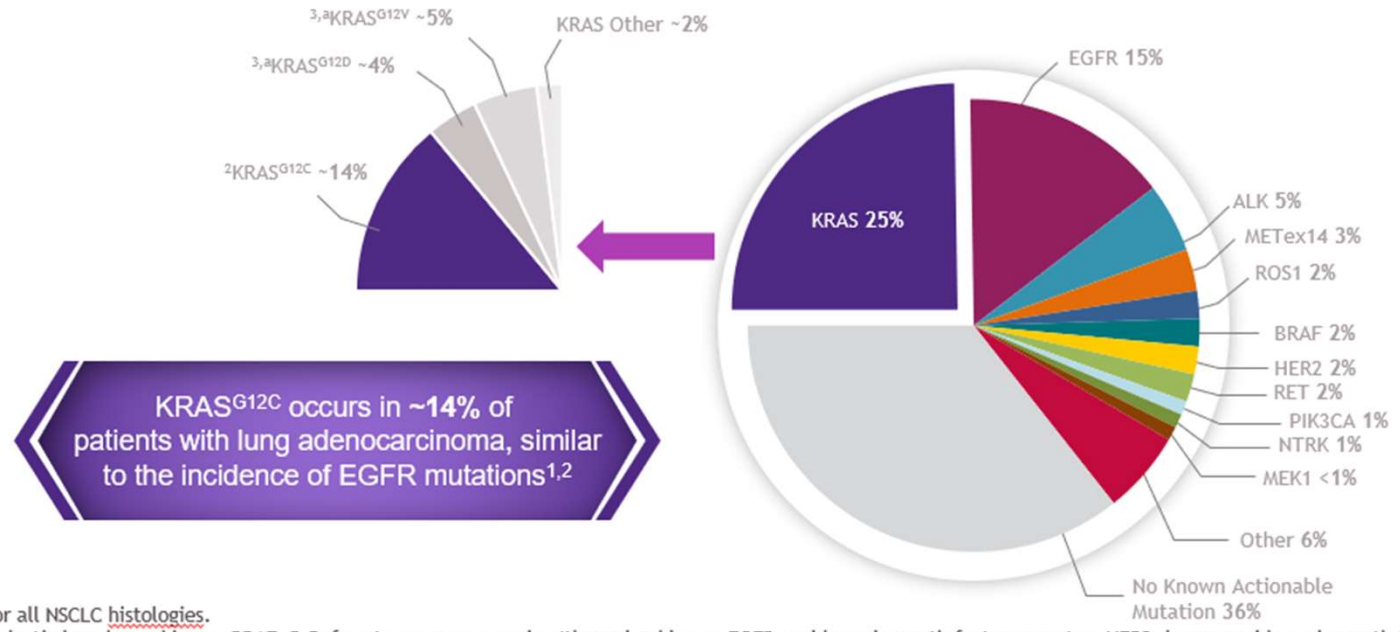
New Checkpoints



The end of the checkpoint era?

KRAS is the Most Prevalent Oncogenic Driver in NSCLC

KRAS mutations account for 25% of mutations in lung adenocarcinoma and are generally mutually exclusive with other oncogenic driver mutations[1]



aValue for all NSCLC histologies.

ALK, anaplastic lymphoma kinase; BRAF, B-Raf proto-oncogene, serine/threonine kinase; EGFR, epidermal growth factor receptor; HER2, human epidermal growth factor receptor 2; KRAS, Kirsten rat sarcoma viral oncogene homolog; MEK1, mitogen-activated protein kinase kinase 1; METex14, mesenchymal-epithelial transition proto-oncogene exon 14; NSCLC, non-small cell lung cancer; NTRK, neurotrophic receptor tyrosine kinase; PIK3CA, phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha; RET, ret proto-oncogene; ROS1, ROS proto-oncogene 1.

1. Pakkala S, et al. JCI Insight. 2018. 2. Nassar AH, et al. N Engl J Med. 2021. 3. Judd J, et al. Mol Cancer Ther. 2021.

End of 2023

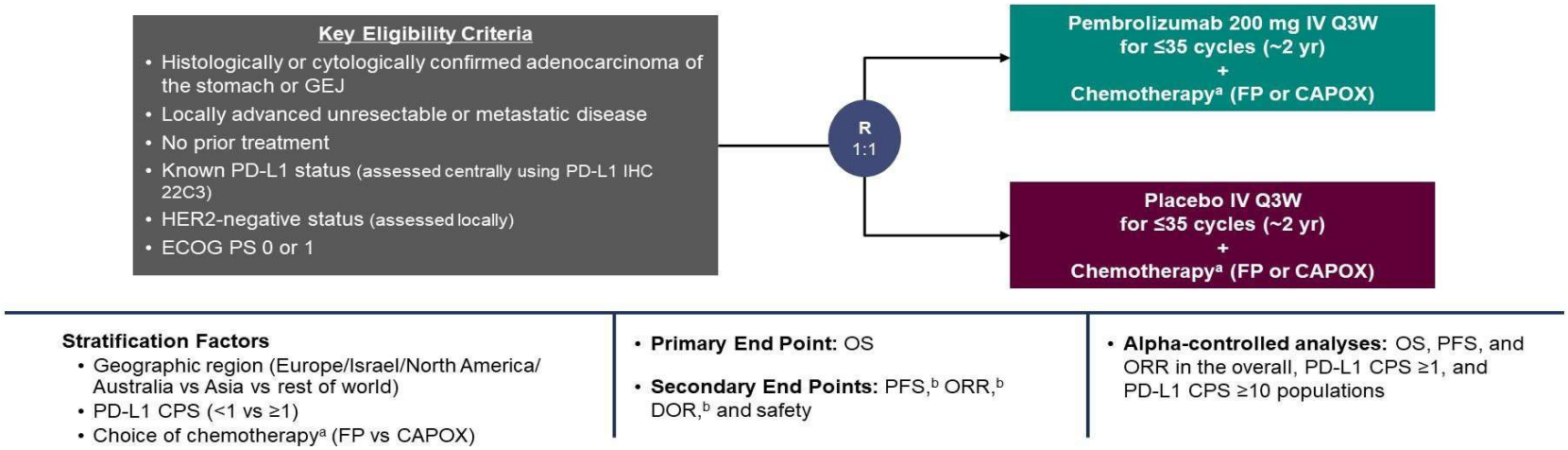
December 18, 2023

MERCK

European Commission Approves Merck's KEYTRUDA® (pembrolizumab) Plus Chemotherapy for New First-Line Indications in Advanced HER2-Negative Gastric or GEJ Adenocarcinoma in Tumors Expressing PD-L1 (CPS ≥1) and Advanced Biliary Tract Cancer

End of 2023

KEYNOTE-859 Study Design
Randomized, Double-Blind, Phase 3 Trial



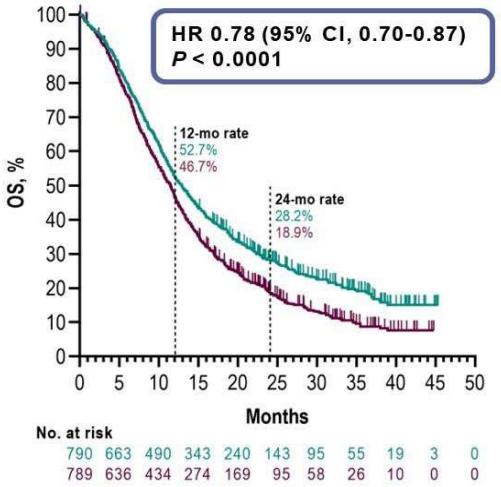
[a] FP: 5-fluorouracil 800 mg/m²/day IV continuous on days 1-5 Q3W + cisplatin 80 mg/m² IV Q3W. CAPOX: capecitabine 1000 mg/m² orally twice daily on days 1-14 Q3W + oxaliplatin 130 mg/m² IV Q3W. Cisplatin and oxaliplatin could have been limited to 6 cycles as per local country guidelines.
[b] Assessed per RECIST v1.1 by blinded, independent central review.
ClinicalTrials.gov number, NCT03675737.

End of 2023

Primary Endpoint: OS

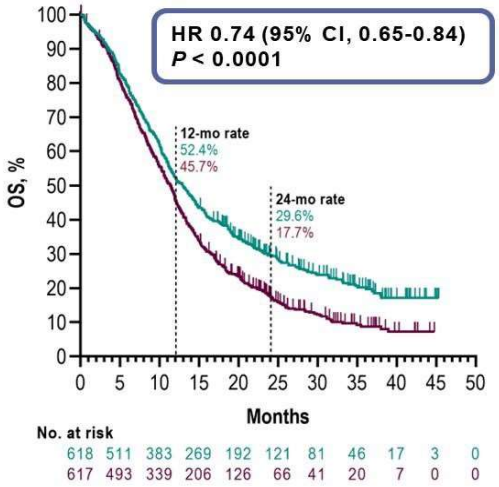
Overall[1]

	Pts w/ Event	Median (95% CI), mo
Pembro + chemo	76.3%	12.9 (11.9-14.0)
Placebo + chemo	84.4%	11.5 (10.6-12.1)



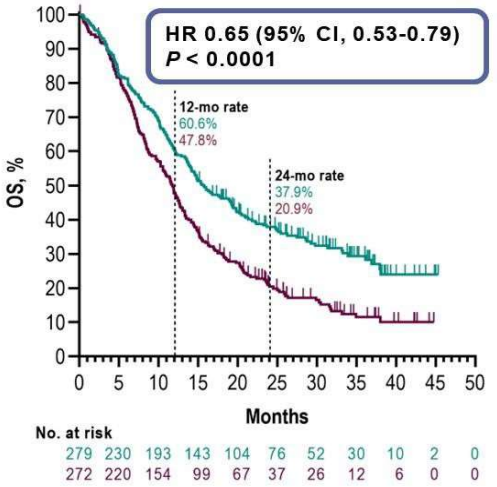
PD-L1 CPS ≥1

	Pts w/ Event	Median (95% CI), mo
Pembro + chemo	75.1%	13.0 (11.6-14.2)
Placebo + chemo	85.3%	11.4 (10.5-12.0)



PD-L1 CPS ≥10

	Pts w/ Event	Median (95% CI), mo
Pembro + chemo	67.4%	15.7 (13.8-19.3)
Placebo + chemo	83.1%	11.8 (10.3-12.7)



1. Rha SY et al. *Ann Oncol* 2023;34:319-320.
Data cutoff date: October 3, 2022.

Jänner 2024

January 16, 2024

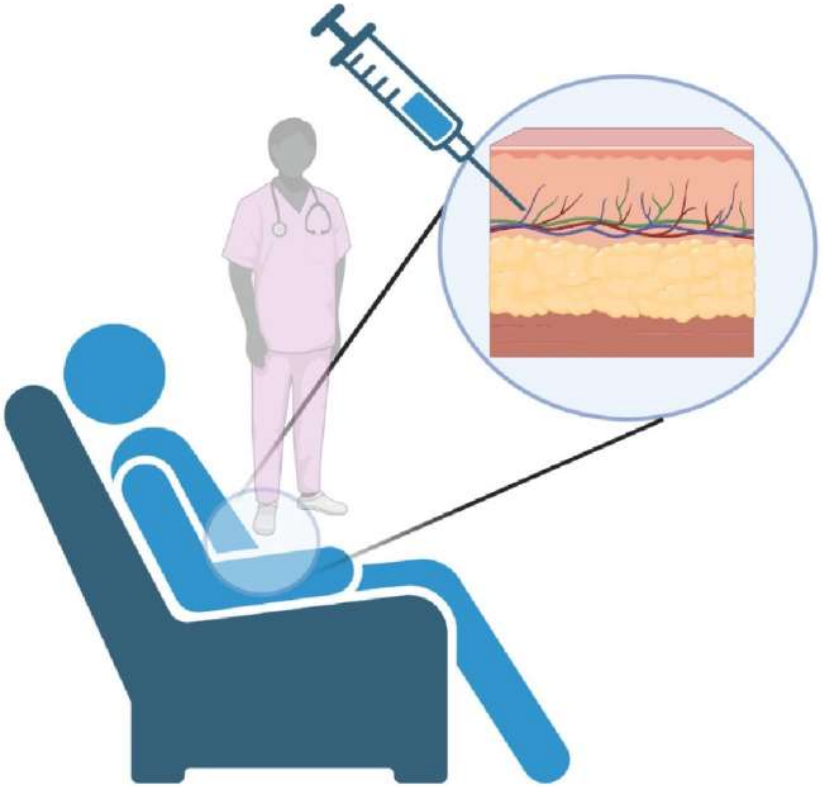
European Commission approves Roche's Tecentriq SC, the EU's first PD-(L)1 cancer immunotherapy subcutaneous injection for multiple cancer types

Roche

The SC formulation uses recombinant human hyaluronidase PH20 enzyme (frequently used in other SC administered cancer medicines) to enable effective delivery. Administration takes approximately 7 minutes (most injections taking between 4 and 8 minutes), offering a significant improvement in administration time (30–60 minutes) compared with the IV formulation but still requiring healthcare professional supervision during this period[iv]. Notably, this market authorization covers all indications previously approved for the IV formulation and can be administered as monotherapy (e.g., urothelial cancer) or in combination with other anticancer therapies, including chemotherapy (e.g., nab-paclitaxel in breast cancer) and targeted therapies (e.g., bevacizumab in hepatocellular carcinoma).*

*Hadfield MJ (2024) Trends in Cancer

Jänner 2024



Advantage: preferred by patients (up to 90% of patients prefer subcutaneous rituximab/trastuzumab compared to intravenous administration)

Advantage: reduced administration time (e.g. shorter infusion, chair and preparation time)

Advantage: reduction in ancillary costs and time (e.g. shorter administration time and venous cannulation)

Disadvantage: increased risk of anti-drug antibody formation (e.g. lower treatment efficacy)

Disadvantage: variable pharmacokinetics (e.g. reduced bioavailability and need to personalize individual dosage)

Advantage: lower risk of immunogenicity (e.g. lower amounts of anti-drug antibodies)

Advantage: ideal for higher volume infusion (e.g. when combined with chemotherapy or other immune checkpoint inhibitors)

Advantage: lower dosage (e.g. lower dose for intravenous atezolizumab [1200 mg] versus subcutaneous atezolizumab [1875mg])

Disadvantage: longer infusion time (e.g. 60 minutes for intravenous atezolizumab versus 7 minutes for subcutaneous atezolizumab)

Disadvantage: potentially higher cost (e.g. higher dosage may mean drugs are more expensive)

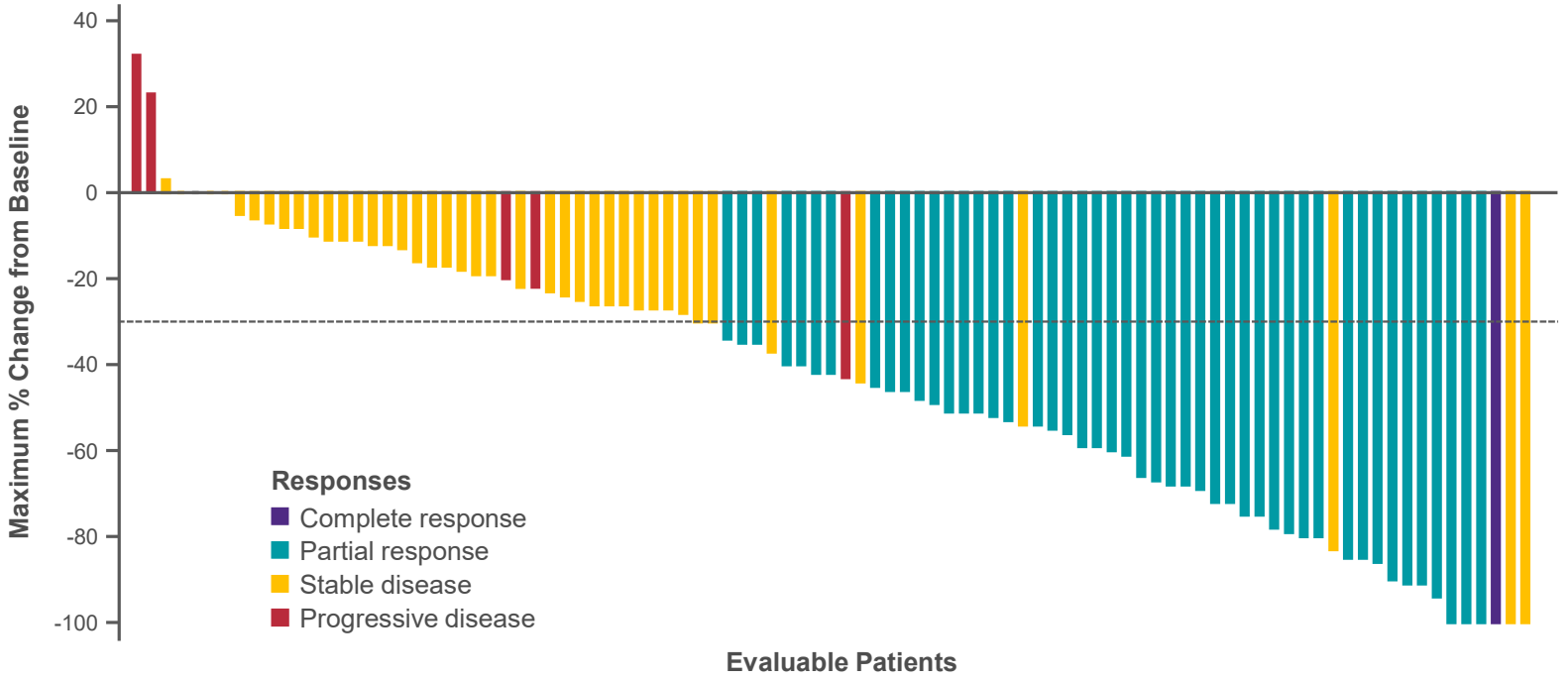
Jänner 2024

European Commission Approves Adagrasib in KRAS G12C-Mutated NSCLC

January 11, 2024

*Hadfield MJ (2024) Trends in Cancer

Adagrasib in Previously Treated Patients with KRAS^{G12C}-Mutated NSCLC: Best Tumor Change From Baseline



- Objective responses were observed in 43% (95% CI, 33.5–52.6); DCR was 80% (95% CI, 70.8–86.5)
- Responses were deep with 75% of responders achieving >50% tumor reduction

Data as of October 15, 2021 (median follow-up: 12.9 months).
BICR, blinded independent central review; CI, confidence interval; DCR, disease control rate; NSCLC, non-small cell lung cancer. All results based on BICR. Responses include target lesion tumor regression, as well as non-target lesion assessment.
Janne PA, et al. N Engl J Med 2022

März 2024

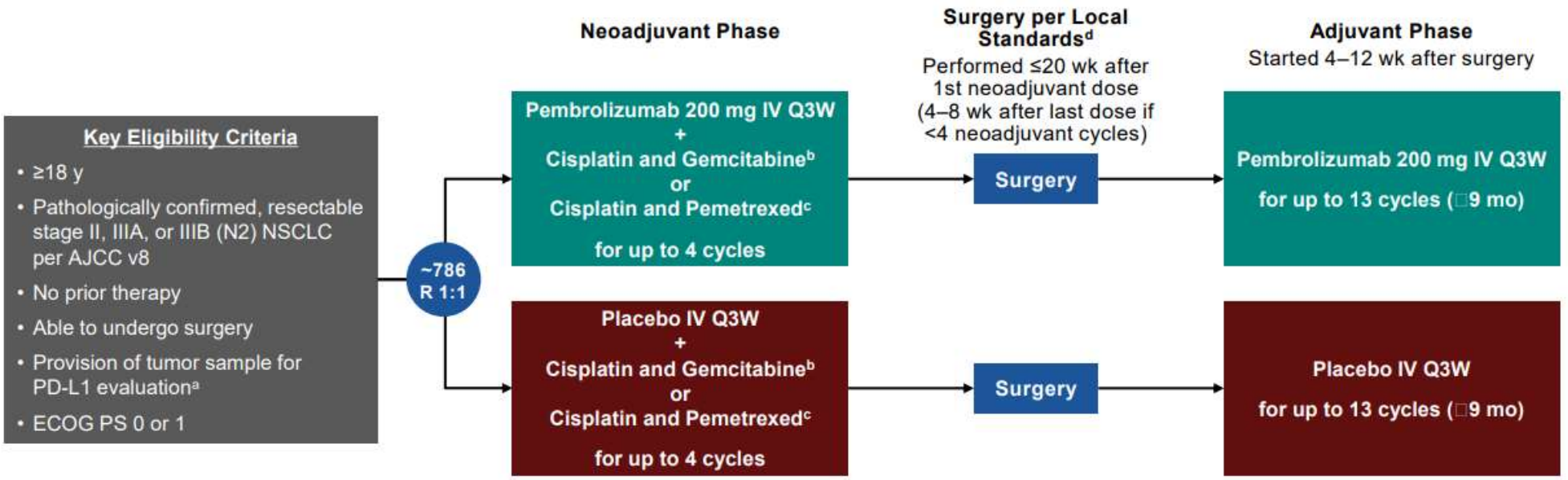
March 28, 2024

MERCK

European Commission Approves Merck's KEYTRUDA® (pembrolizumab) Plus Chemotherapy as Neoadjuvant Treatment, Then Continued as Monotherapy as Adjuvant Treatment, for Resectable Non-Small Cell Lung Cancer (NSCLC) at High Risk of Recurrence in Adults

KEYNOTE-671 Study Design

Randomized, Double-Blind, Phase 3 Trial



Stratification Factors

- Disease stage (II vs III)
- PD-L1 TPS[a] (<50% vs ≥50%)
- Histology (squamous vs nonsquamous)
- Geographic region (East Asia vs not East Asia)

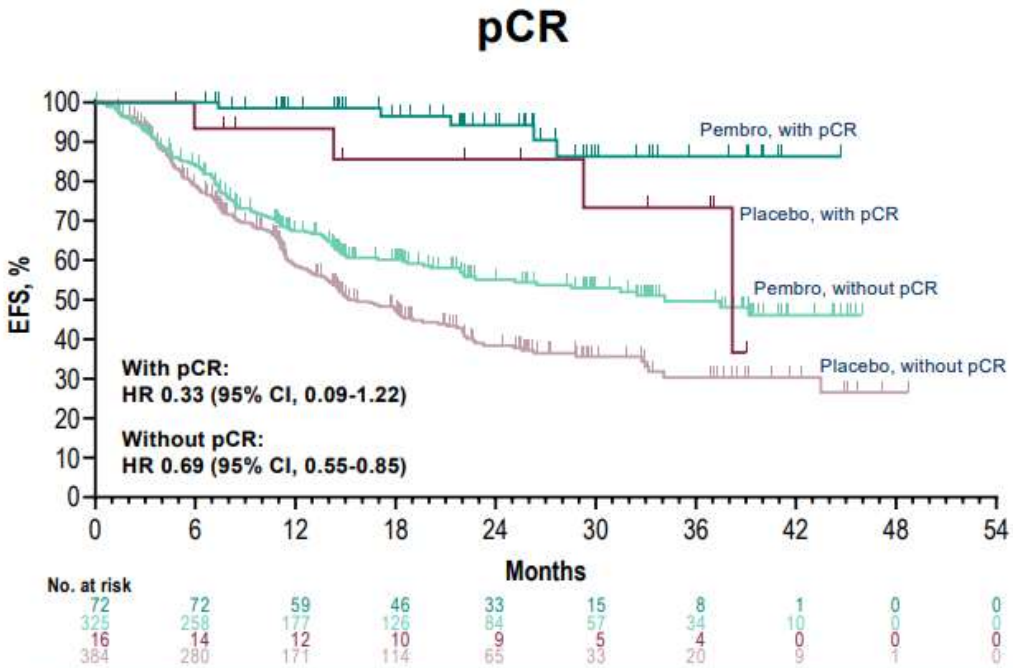
Dual primary end points: EFS per investigator review and OS

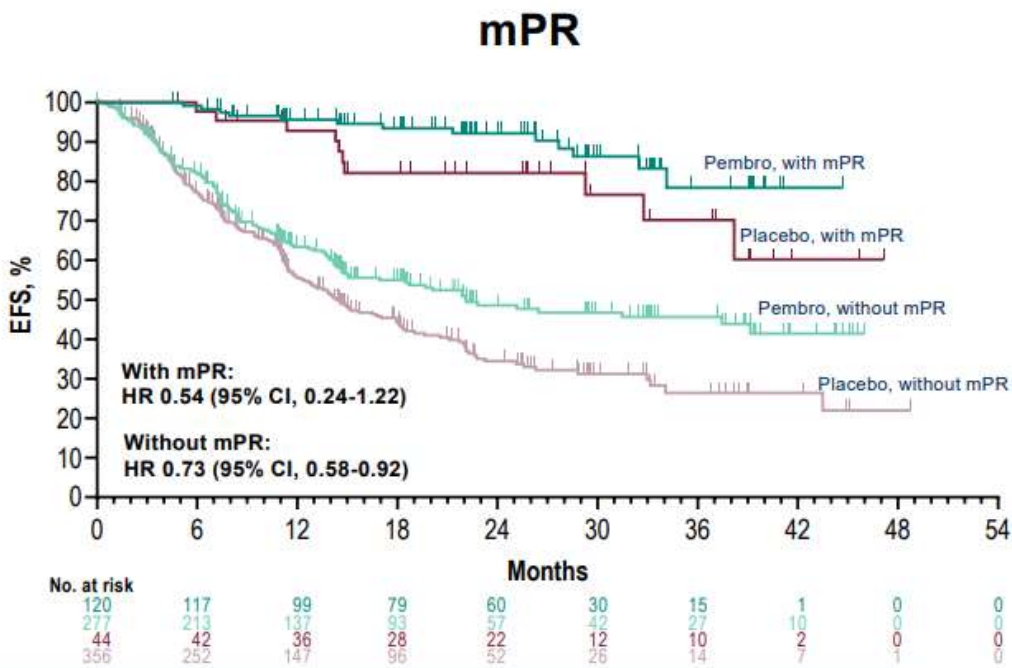
Key secondary end points: mPR and pCR per blinded, independent pathology review and safety

Pathologic regression categorization: Patients who underwent surgery and had tissue evaluable for blinded independent pathology review were categorized by %RVT in the primary lung tumor and sampled lymph nodes

[a]Assessed at a central laboratory using PD-L1 IHC 22C3 pharmDx. [b]Cisplatin 75 mg/m^2 IV Q3W + gemcitabine 1000 mg/m^2 IV on days 1 and 8 Q3W (squamous histology only). [c]Cisplatin 75 mg/m^2 IV Q3W + pemetrexed 500 mg/m^2 IV Q3W (nonsquamous histology only). [d]Radiotherapy was to be administered to patients with microscopic positive margins, gross residual disease, or extracapsular nodal extension after surgery and to patients who did not undergo planned surgery for any reason other than local progression or metastatic disease. ClinicalTrials.gov identifier: NCT03425643.

Event-Free Survival Among Patients With pCR or mPR[a,1]





Objective of this analysis was to evaluate efficacy of perioperative pembrolizumab across different RVT cutpoints, beyond pCR and mPR

[1]Wakelee H et al. *N Engl J Med* 2023;389:491–503.
[a]Exploratory analysis. pCR defined as absence of residual invasive cancer in resected primary tumor and lymph nodes (ypT0/Tis ypN0). [b]mPR defined as ≤10% viable tumor cells in resected primary tumor and lymph nodes. EFS defined as time from randomization to first occurrence of local progression precluding planned surgery, unresectable tumor, progression or recurrence per RECIST v1.1 by investigator assessment, or death from any cause. Data cutoff date for IA1: July 29, 2022.

April 2024

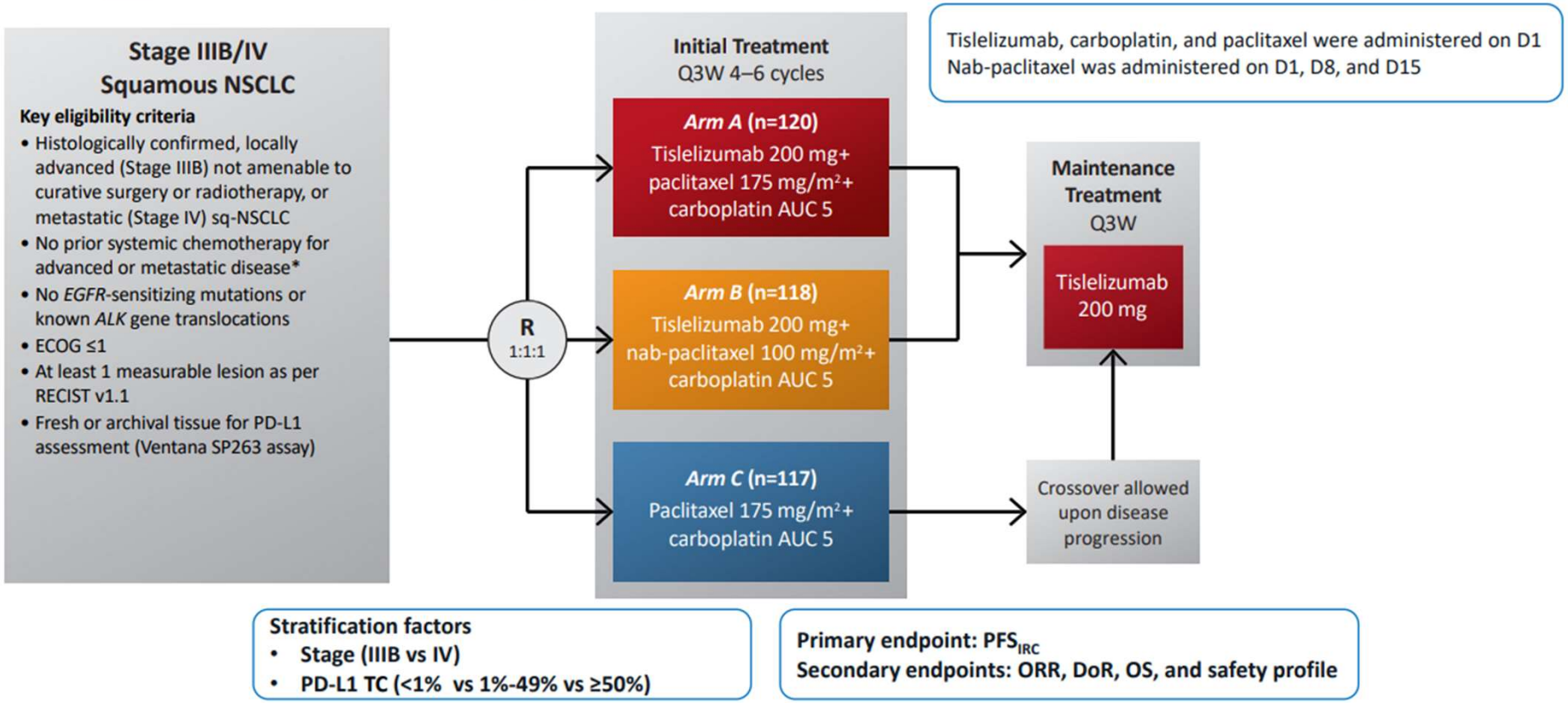
Apr 23, 2024

BeiGene Receives European Commission Approval for Tislelizumab as Treatment for Non-Small Cell Lung Cancer

The approved indications for tislelizumab are:

- In combination with carboplatin and either paclitaxel or nab-paclitaxel for the first-line treatment of adult patients with squamous NSCLC who have locally advanced NSCLC and are not candidates for surgical resection or platinum-based chemoradiation, or metastatic NSCLC.
- In combination with pemetrexed and platinum-containing chemotherapy for the first-line treatment of adult patients with non-squamous NSCLC whose tumors have PD-L1 expression on ≥50% of tumor cells with no EGFR or ALK positive mutations and who have locally advanced NSCLC and are not candidates for surgical resection or platinum-based chemoradiation, or metastatic NSCLC.
- As monotherapy for the treatment of adult patients with locally advanced or metastatic NSCLC after prior platinum-based therapy. Patients with EGFR mutant or ALK positive NSCLC should also have received targeted therapies before receiving tislelizumab.

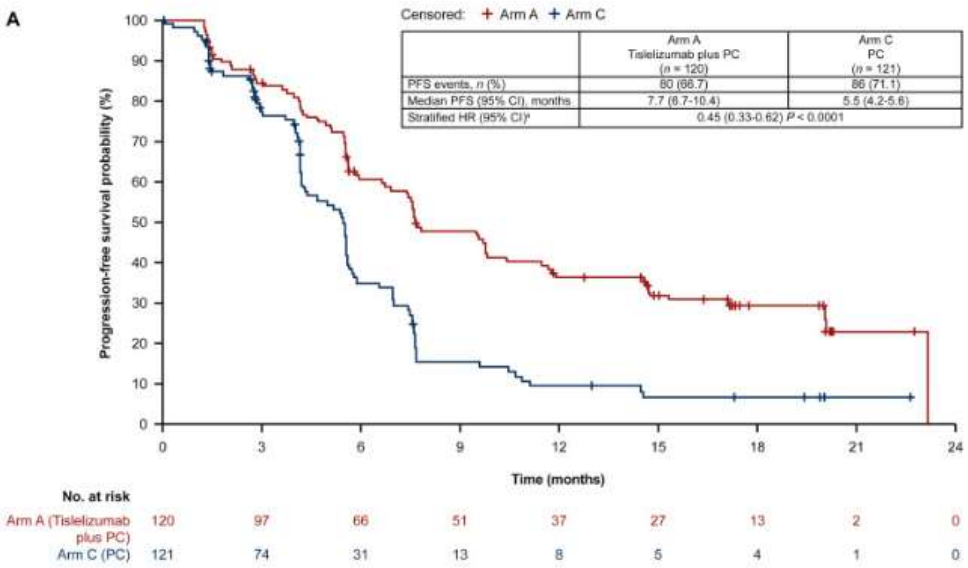
RATIONALE 307 Study (BGB-A317-307)

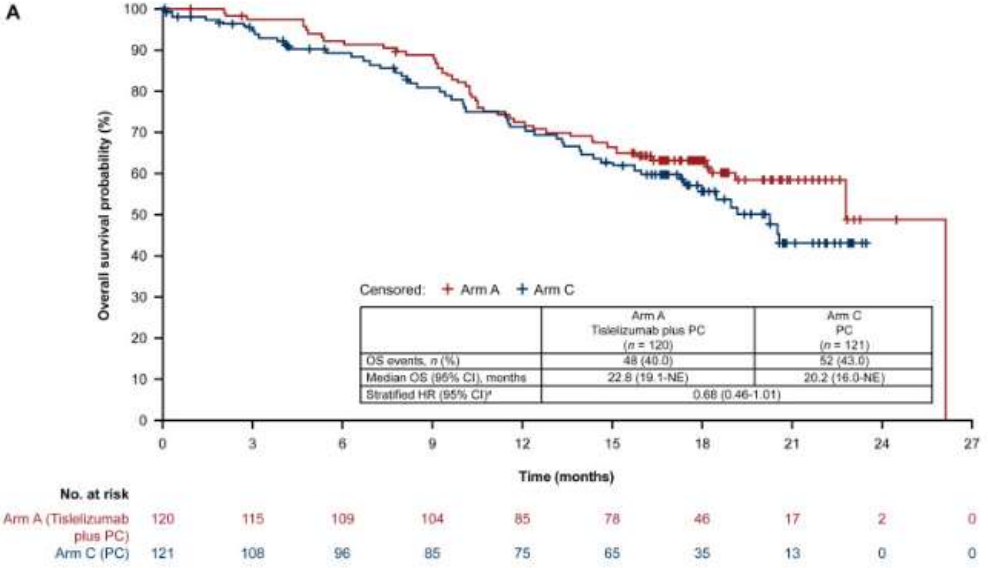


*Patients receiving prior neoadjuvant or adjuvant chemotherapy, radiotherapy, or chemoradiotherapy with curative intent for non-metastatic disease must have experienced a disease-free interval of ≥6 months from the last dose of chemotherapy and/or radiotherapy prior to randomization.

Abbreviations: D, day; DoR, duration of response; ECOG, Eastern Cooperative Oncology Group; IRC, independent review committee; nab, nanoparticle albumin-bound; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PD-L1, programmed death-ligand 1; PFS, progression-free survival; Q3W, every 3 weeks; R, randomized; RECIST, response evaluation criteria in solid tumors; sq, squamous; TC, tumor cell.

RATIONALE 307 Study





Mai 2024

Bristol Myers Squibb

See All Press Releases > Sign up for Email Alerts >

Bristol Myers Squibb Receives European Commission Approval for Opdivo® (nivolumab) in Combination with Cisplatin and Gemcitabine for the First-Line Treatment of Adult Patients with Unresectable or Metastatic Urothelial Carcinoma

05/29/2024

CATEGORY: Corporate/Financial News

Approval based on results from CheckMate -901, the first Phase 3 trial in this patient population with an immunotherapy-chemotherapy combination to demonstrate survival benefit versus standard-of-care chemotherapy alone

First concurrent immunotherapy-chemotherapy combination approved for this patient population in the European Union

PRINCETON, N.J.--(BUSINESS WIRE)-- Bristol Myers Squibb (NYSE: BMY) today announced that the European Commission (EC) has approved *Opdivo®* (nivolumab) in combination with cisplatin and gemcitabine for the first-line treatment of adult patients with unresectable or metastatic urothelial carcinoma (UC). With this approval, *Opdivo* in combination with cisplatin and gemcitabine becomes the first concurrent immunotherapy-chemotherapy approved for the treatment of adult patients with unresectable or metastatic UC in the first-line setting in the European Union.

Study design

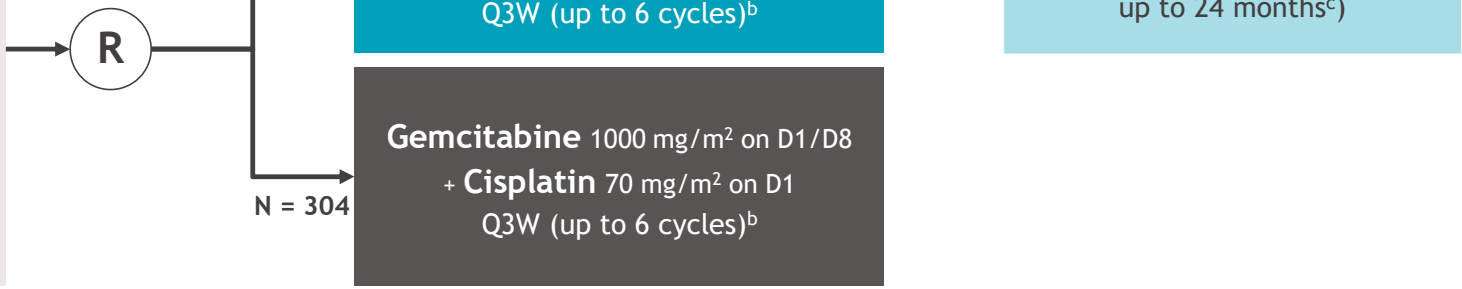
- NIVO + GC versus GC in cisplatin-eligible patients[a]

Key inclusion criteria

- Age ≥ 18 years
- Previously untreated, unresectable or mUC involving the renal pelvis, ureter, bladder, or urethra
- Cisplatin eligible
- ECOG PS of 0-1

Stratification factors:

- Tumor PD-L1 expression (≥ 1% vs < 1%)
- Liver metastases (yes vs no)



Median (range) study follow-up, 33.6 (7.4–62.4) months

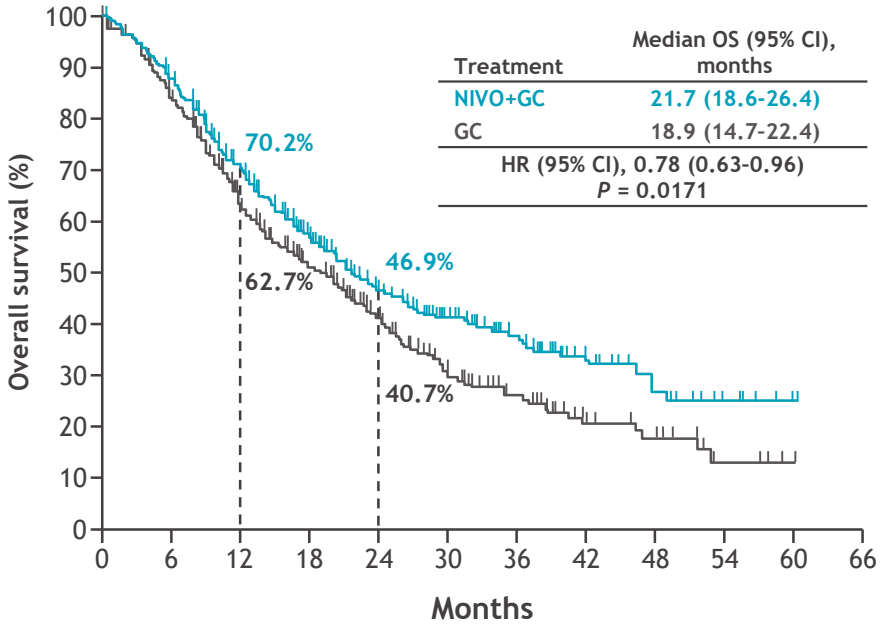
Primary endpoints: OS, PFS per BICR
Key secondary endpoints: OS and PFS by PD-L1 ≥ 1%,[d] HRQoL
Key exploratory endpoints: ORR per BICR, safety

Current analysis: baseline characteristics, treatment exposure, efficacy, duration of response, subsequent therapy, and safety outcomes in all responders

[a]Further CheckMate 901 trial design details are available at https://clinicaltrials.gov/ct2/show/NCT03036098. [b]Patients who discontinued cisplatin could be switched to GC for the remainder of the platinum doublet cycles (up to 6 in total). [c]A maximum of 24 months from first dose of NIVO administered as part of the NIVO + GC combination. [d]PD-L1 status was defined by the percentage of positive tumor cell membrane staining in a minimum of 100 tumor cells that could be evaluated with the use of the PD-L1 IHC 28-8 pharmDx immunohistochemical assay (Dako, Santa Clara, CA).

OS and PFS per BICR in ITT population (primary endpoints)[1]

OS[a]

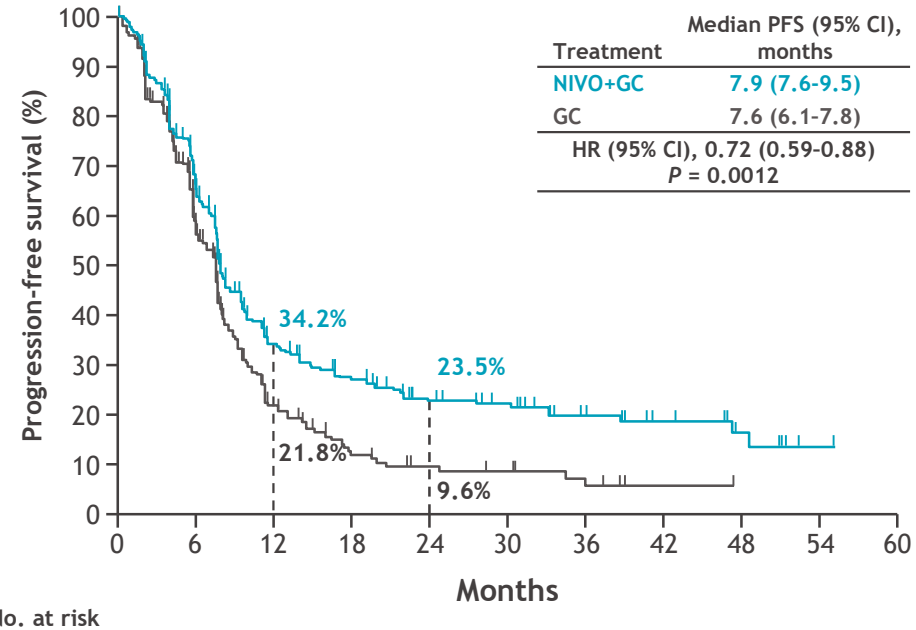


Treatment	Median OS (95% CI), months
NIVO+GC	21.7 (18.6-26.4)
GC	18.9 (14.7-22.4)
HR (95% CI), 0.78 (0.63-0.96) *P* = 0.0171	

No. at risk

NIVO+GC	304	264	196	142	97	69	48	25	15	7	2	0
GC	304	242	166	122	82	49	33	17	13	4	1	0

PFS per BICR[b]



Treatment	Median PFS (95% CI), months
NIVO+GC	7.9 (7.6-9.5)
GC	7.6 (6.1-7.8)
HR (95% CI), 0.72 (0.59-0.88) *P* = 0.0012	

No. at risk

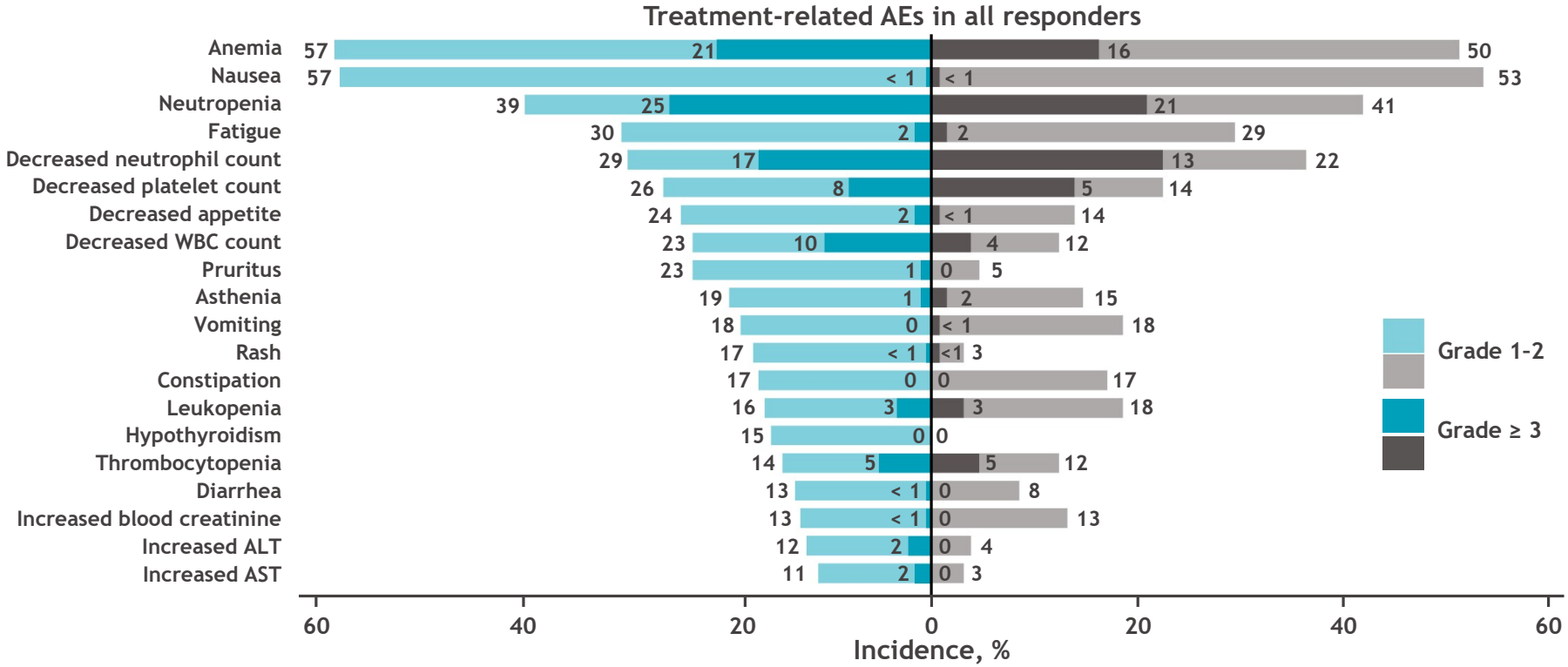
NIVO+GC	304	179	82	57	41	31	19	11	6	1	0	
GC	304	119	35	17	10	8	5	1	0	0	0	

Median (range) study follow-up was 33.6 (7.4–62.4) months.
[a]OS was estimated in all randomized patients and defined as time from randomization to death from any cause. For patients without documented death, OS was censored on the last date the patient was known to be alive. For randomized patients with no follow-up, OS was censored at randomization. [b]PFS was estimated in all randomized patients and defined as time from randomization to first documented disease progression (per BICR assessments using RECIST v1.1) or death due to any cause, whichever occurred first. Patients who did not progress or die were censored at last evaluable tumor assessment. Patients without on-study tumor assessments who did not die were censored at randomization. Patients who started any subsequent anticancer therapy without prior reported progression were censored at last evaluable tumor assessment before initiation of subsequent therapy.

1. van der Heijden MS, et al. *N Engl J Med* 2023;389:1778-1789.

Treatment-related AEs

Treatment-related AE, %[a]	All treated patients[1]		All responders	
	NIVO+GC (n = 304)	GC (n = 288)	NIVO+GC (n = 175)	GC (n = 131)
Any grade	97	93	100	98
Grade ≥ 3	62	52	68	57



[a]Includes events that occurred in treated patients between first dose and 30 days after last dose of study therapy. Tornado plot displays individual treatment-related AEs occurring at any grade in ≥ 10% of treated patients in either arm.

1. van der Heijden MS, et al. *N Engl J Med* 2023;389:1778-1789.

Juni 2024

2024 ASCO® ANNUAL MEETING

ASCO Gastrointestinal Cancers Symposium

Nivolumab plus ipilimumab vs chemotherapy as first-line treatment for microsatellite instability-high/ mismatch repair-deficient metastatic colorectal cancer: first results of the CheckMate 8HW study

Thierry Andre,[1] Elena Elez,[2] Eric Van Cutsem,[3] Lars Henrik Jensen,[4] Jaafar Bennouna,[5] Guillermo Ariel Mendez,[6] Michael Schenker,[7] Christelle de la Fouchardiere,[8] Maria Luisa Limon,[9] Takayuki Yoshino,[10] Jin Li,[11] Heinz-Josef Lenz,[12] Jose Manzano Mozo,[13] Giampaolo Tortora,[14] Rocio Garcia-Carbonero,[15] Elvis Cela,[16] Yingsi Yang,[16] Ming Lei,[16] Lixian Jin,[16] Sara Lonardi[17]

[1]Sorbonne Université and Hôpital Saint Antoine, Assistance Publique Hôpitaux de Paris, Paris, France; [2]Vall d'Hebron University Hospital and Institute of Oncology (VHIO), Barcelona, Spain; [3]University Hospitals Gasthuisberg and University of Leuven (KU Leuven), Leuven, Belgium; [4]University Hospital of Southern Denmark, Vejle Hospital, Vejle, Denmark; [5]Centre Hospitalier Universitaire de Nantes, Nantes, France; [6]Hospital Universitario Fundacion Favaloro, Buenos Aires, Argentina; [7]Centrul de Oncologie Sf Nectarie, Craiova, Romania; [8]Centre Léon Bérard, Lyon Cedex, France; [9]Hospital Universitario Virgen del Rocío, Sevilla, Spain; [10]National Cancer Center Hospital East, Chiba, Japan; [11]Shanghai East Hospital, Shanghai, China; [12]University of Southern California Norris Comprehensive Cancer Center, Los Angeles, CA; [13]Institut Català d'Oncologia, Badalona, Spain; [14]Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy; [15]Hospital Universitario 12 de Octubre Imas12, UCM, Madrid, Spain; [16]Bristol Myers Squibb, Princeton, NJ; [17]Istituto Oncologico Veneto IOV-IRCCS, Padua, Italy

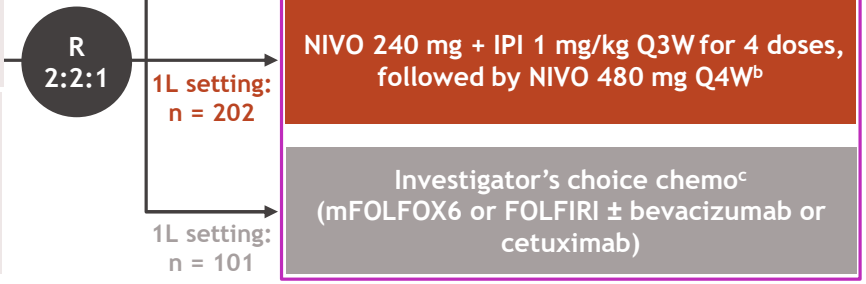
Abstract number LBA768

CheckMate 8HW study design

- CheckMate 8HW is a randomized, multicenter, open-label phase 3 study[a]

Key eligibility criteria:
- Histologically confirmed unresectable or metastatic CRC
- MSI-H/dMMR status by local testing
- ECOG PS 0 or 1

Stratification factors:
- Prior lines of treatment (0 vs 1 vs ≥ 2)
- Primary tumor location (right vs left)



Treatment until disease progression, unacceptable toxicity, withdrawal of consent (all arms), or a maximum treatment duration of 2 years (NIVO and NIVO + IPI arms only)

Dual primary endpoints in patients with centrally confirmed MSI-H/dMMR status[d]:
- PFS by BICR[e] (NIVO + IPI vs chemo in the 1L setting)
- PFS by BICR[e] (NIVO + IPI vs NIVO across all lines)

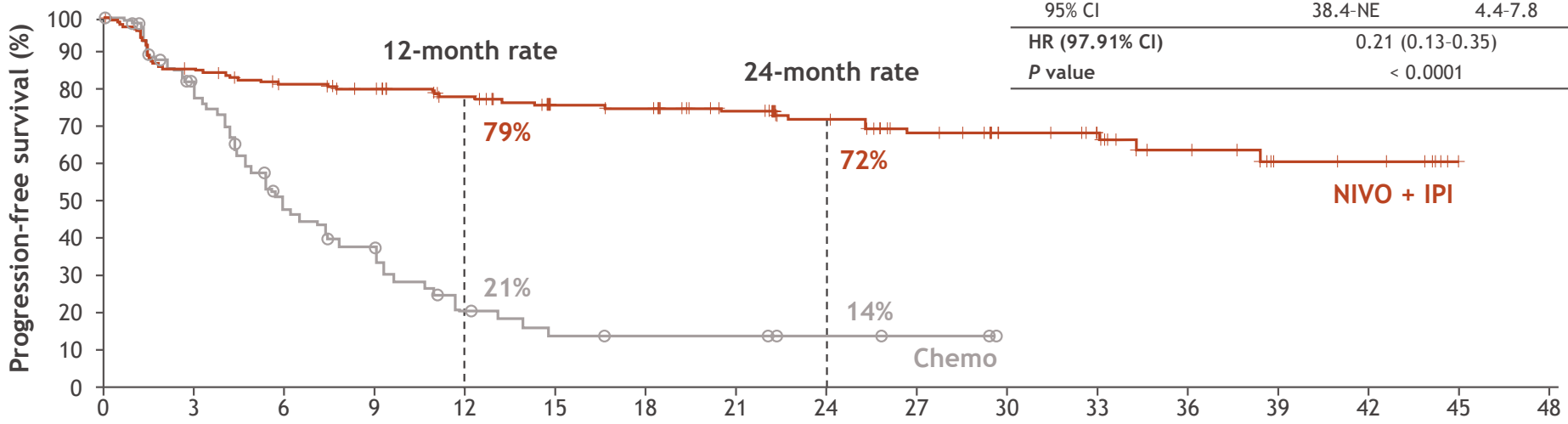
Other select endpoints:
- Safety
- OS; ORR by BICR[e]; PROs

- At data cutoff (October 12, 2023), the median follow-up[f] was 24.3 months

[a]ClinicalTrials.gov. NCT04008030. [b]Patients with ≥ 2 prior lines are randomized only to the NIVO or NIVO + IPI arms. [c]Patients receiving investigator's choice of chemotherapy are eligible to receive NIVO + IPI upon progression (crossover treatment). [d]Confirmed using either immunohistochemistry and/or polymerase chain reaction-based tests. [e]Evaluated using RECIST v1.1. [f]Time between randomization and last known date alive or death.

Progression-free survival

1L centrally confirmed MSI-H/dMMR	NIVO + IPI (n = 171)	Chemo (n = 84)
Median PFS,[a,b] mo	NR	5.9
95% CI	38.4-NE	4.4-7.8
HR (97.91% CI)	0.21 (0.13-0.35)	
P value	< 0.0001	



No. at risk																	
NIVO + IPI	171	144	132	122	108	95	92	77	64	53	42	37	22	10	9	1	0
Chemo	84	53	29	20	10	6	5	5	3	2	0	0	0	0	0	0	0

- PFS benefit with NIVO + IPI vs chemo was robust and consistent across the sensitivity analyses, including PFS by BICR in 1L all randomized patients (HR, 0.32; 95% CI, 0.23–0.46)

[a]Per BICR. [b]Median follow-up, 24.3 months.

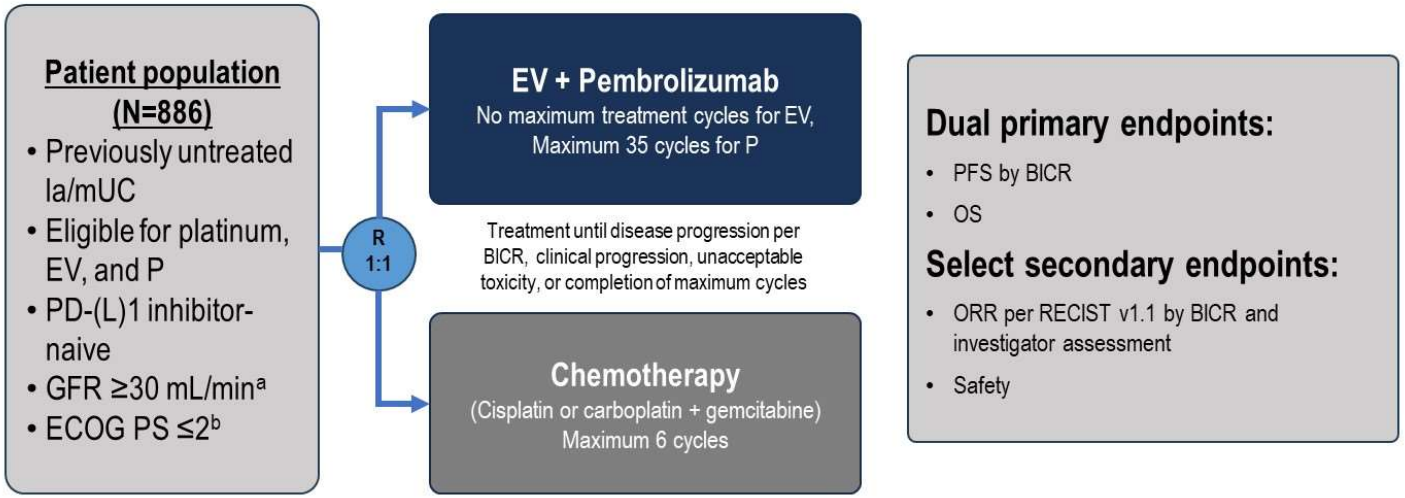
September 2024

September 03, 2024

MERCK

European Commission Approves Merck's KEYTRUDA® (pembrolizumab) Plus Padcev® (enfortumab vedotin-ejfv) as First-Line Treatment of Unresectable or Metastatic Urothelial Carcinoma in Adults

EV-302/KEYNOTE-A39 (NCT04223856)



Dual primary endpoints:

- PFS by BICR
- OS

Select secondary endpoints:

- ORR per RECIST v1.1 by BICR and investigator assessment
- Safety

Prespecified subgroups:

- **Stratification factors**
  - **Cisplatin eligibility (eligible, ineligible)**
  - **PD-L1 expression (low, high)**
  - **Liver metastases (present, absent)**
- **Age (<65, ≥65 years old)**
- **Region (North America, Europe, Rest of World)**
- **Sex (female, male)**
- **Race (white, other)**
- **ECOG PS at baseline (0, 1-2)**
- **Visceral metastases vs. lymph node only metastases**
- **Primary disease site of origin (upper tract, lower tract)**
- **Renal function (normal, mild, moderate, severe)**

Cisplatin eligibility and assignment/dosing of cisplatin vs carboplatin were protocol-defined; patients received 3-week cycles of EV (1.25 mg/kg; IV) on Days 1 and 8 and P (200 mg; IV) on Day 1

Statistical plan for analysis: the first planned analysis was performed after approximately 526 PFS (final) and 356 OS events (interim); if OS was positive at interim, the OS interim analysis was considered final

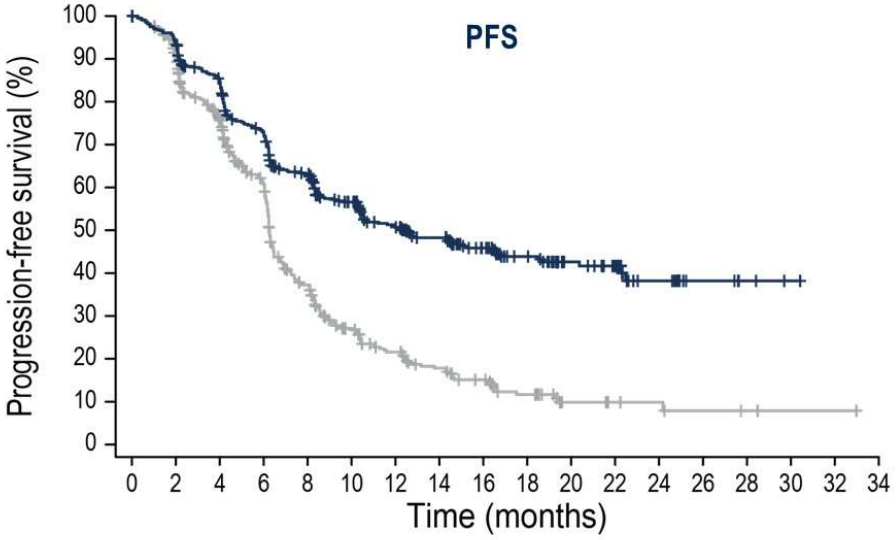
Maintenance therapy was permitted if deemed appropriate by the investigator following completion and/or discontinuation of platinum-containing therapy

Data cutoff: 08 August 2023; FPI: 07 Apr 2020, LPI: 09 Nov 2022

[a]Measured by the Cockcroft-Gault formula, Modification of Diet in Renal Disease, or 24-hour urine
[b]Patients with ECOG PS of 2 were required to also meet additional criteria: hemoglobin ≥10 g/dL, GFR ≥50mL/min, may not have NYHA class III heart failure
BICR, blinded independent central review; ECOG PS, Eastern Cooperative Oncology Group performance status; GFR, glomerular filtration rate; NYHA, New York Heart Association; ORR, objective response rate; PFS, progression-free survival; R, randomization; RECIST, Response Evaluation Criteria in Solid Tumors

EV-302 Summary: PFS per BICR and OS in ITT

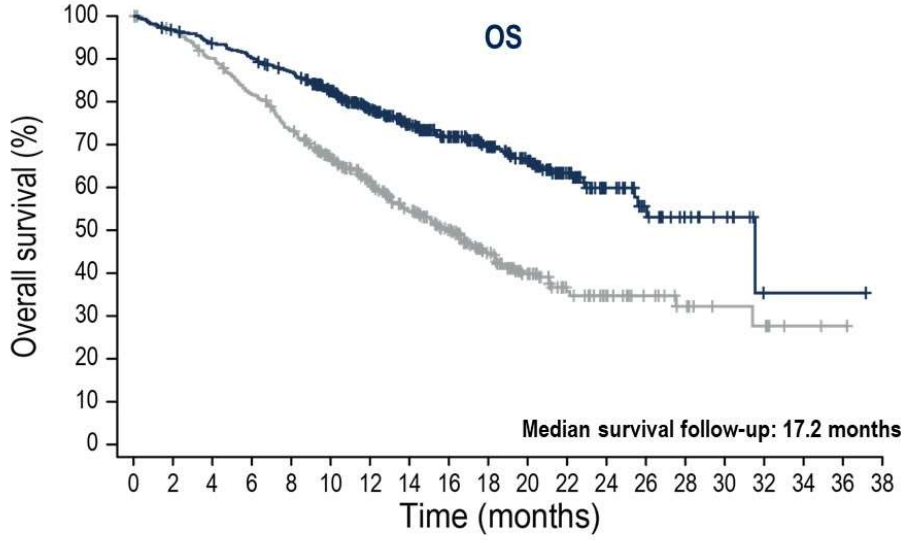
mPFS and mOS were nearly doubled in the EV+P arm compared with chemotherapy



N at risk

EV+P	442	409	361	303	253	204	167	132	102	73	45	33	17	6	3	1
Chemotherapy	444	380	297	213	124	78	56	41	30	19	8	6	5	3	2	1	1

	HR[a] (95% CI)	2-sided P value	mPFS (95% CI), months
EV+P	0.45 (0.38-0.54)	<0.00001	12.5 (10.4-16.6)
Chemotherapy			6.3 (6.2-6.5)



N at risk

EV+P	442	426	409	394	376	331	270	222	182	141	108	67	36	22	12	8	1	1	1
Chemotherapy	444	423	393	356	317	263	209	164	125	90	60	37	25	18	12	7	6	2	1

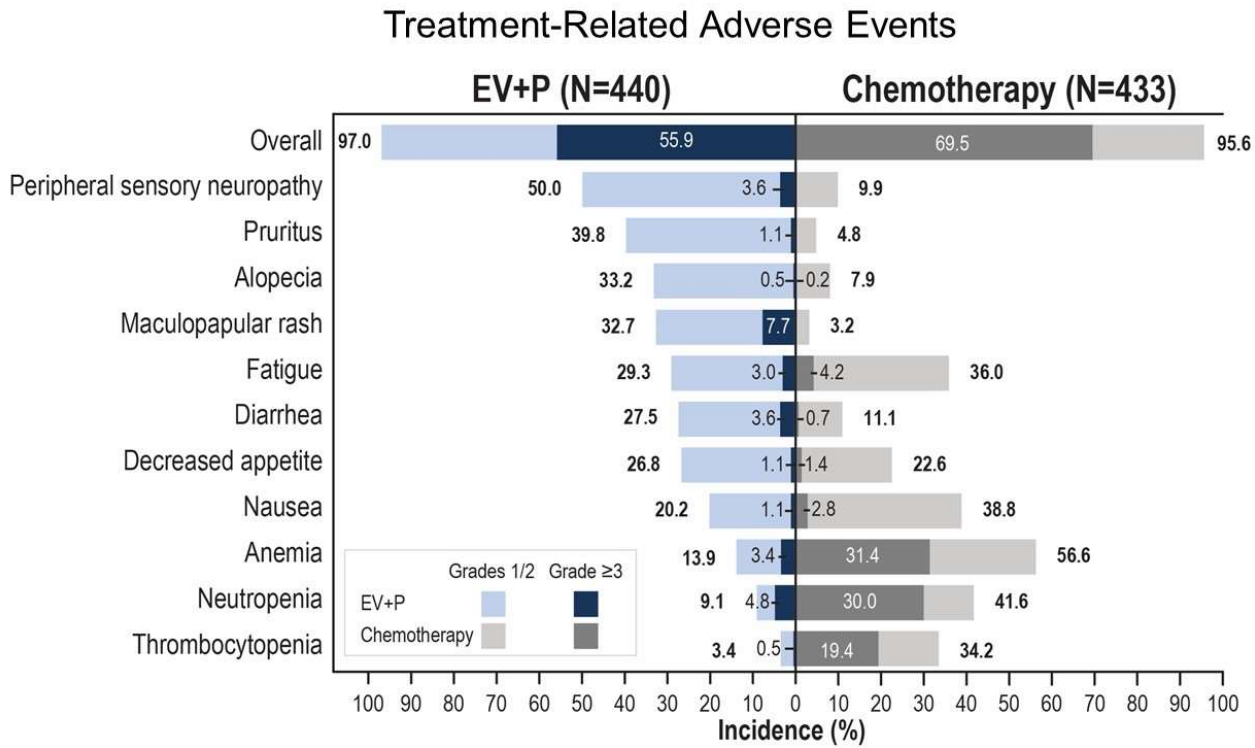
	HR[a] (95% CI)	2-sided P value	mOS (95% CI), months
EV+P	0.47 (0.38-0.58)	<0.00001	31.5 (25.4-NR)
Chemotherapy			16.1 (13.9-18.3)

Powles T. ESMO 2023: Oral presentation. Abstract LBA6.
Data cutoff: 08 August 2023

[a]Calculated using stratified Cox proportional hazards model; a hazard ratio <1 favors the EV+P arm
HR, hazard ratio; ITT, intent-to-treat; mOS, median overall survival; mPFS, median progression-free survival; NR, not reached

EV-302 Summary: Overall Safety

The safety profile of EV+P was generally manageable with no new safety signals observed



- Grade ≥3 events were observed in 56% in EV+P and 70% in chemotherapy
- No new safety signals were seen for EV AESIs or pembrolizumab AEOSIs

TRAEs leading to death (per investigator):
EV+P: 4 (0.9%)
- Asthenia
- Diarrhea
- Immune-mediated lung disease
- Multiple organ dysfunction syndrome

Chemotherapy: 4 (0.9%)
- Febrile neutropenia
- Myocardial infarction
- Neutropenic sepsis
- Sepsis

Powles T. ESMO 2023: Oral presentation. Abstract LBA6.
Data cutoff: 08 August 2023

AESI, adverse event of special interest (EV); AEOSI, adverse event of special interest (pembrolizumab); TRAE, treatment-related adverse event

September 2024

Junshi Biosciences

君实生物 TopAlliance

OncLive
Bringing the Global Oncology Community Together

News ▾ Media ▾ Conferences ▾ Events ▾ Partners Publications ▾ CME/CE

Choose Specialty ▾ **Spotlight -** In-person and virtual events just for HCPs

News | Article | September 25, 2024

Toripalimab Plus Chemo Wins European Approval for Nasopharyngeal Carcinoma and Esophageal Squamous Cell Carcinoma

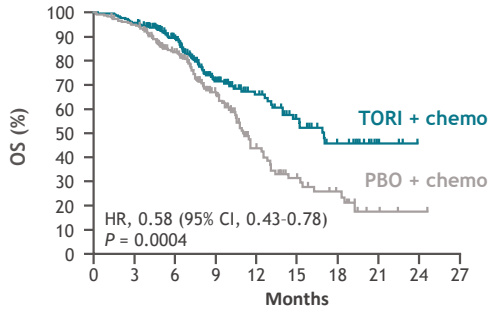
Author(s): Chris Ryan

Fact checked by: Kyle Doherty

JUPITER-06[5,6]

N = 514
100% SCC
100% China

All patients



No. at risk

TORI + chemo	257	246	171	86	52	31	18	4	0	0
PBO + chemo	257	242	166	79	33	18	11	3	1	0

Extracted from *Cancer Cell*.[6]

- TORI + chemo had a manageable safety profile[6]

5. Xu R-H et al. Presentation at European Society for Medical Oncology (ESMO) Congress; September 16-21, 2021; virtual. Abstract 1373MO. 6. Wang Z-X et al. *Cancer Cell*. 2022;40:277-288.

September 2024

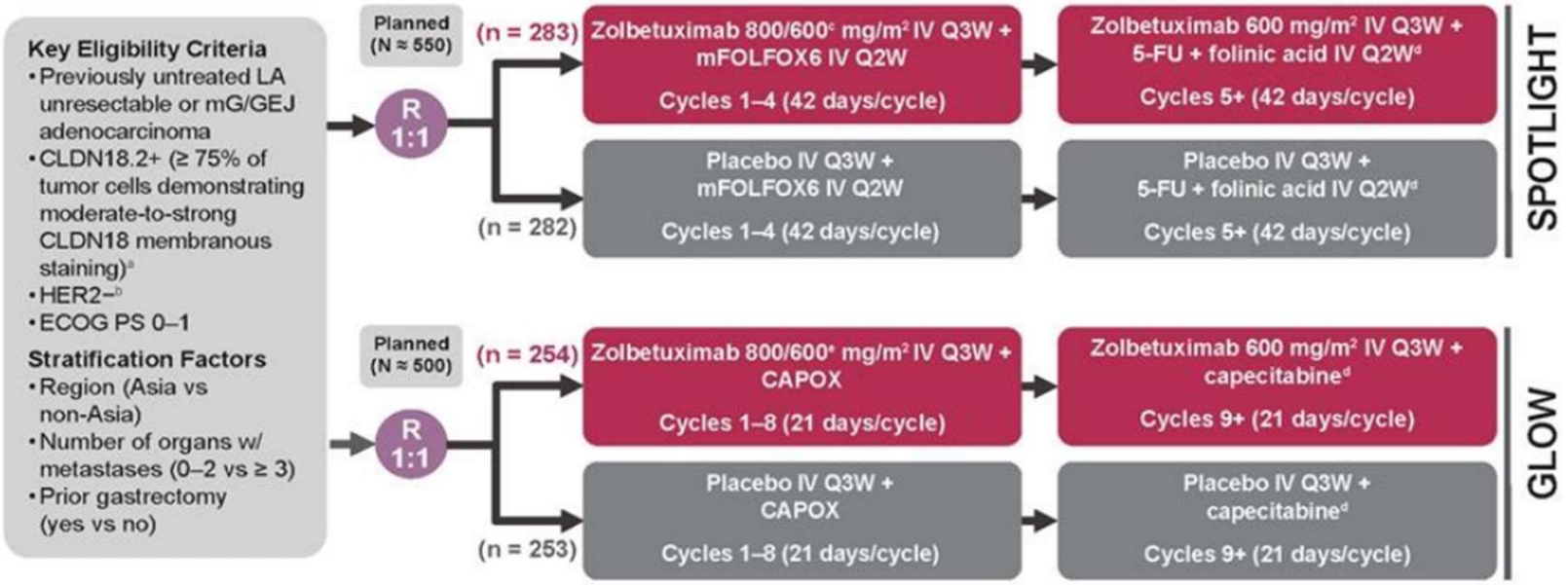
Astellas Receives Approval from the European Commission for VYLOY™ (zolbetuximab) in Combination with Chemotherapy for Advanced Gastric and Gastroesophageal Junction Cancer

Sep 24, 2024

- Zolbetuximab is currently the first and only therapy approved in the European Union to target claudin 18.2, a biomarker positively expressed by 38% of patients with advanced gastric cancer[1,2] -

- Treatment with the claudin 18.2-targeted monoclonal antibody shown to significantly extend both progression-free survival and overall survival in Phase 3 trials[1,2] -

Figure 1. Study Designs of SPOTLIGHT and GLOW: Global, Randomized, Double-Blind, Placebo-Controlled, Phase 3 Trials[1,2]



[a]By central IHC using the VENTANA CLDN18 (43-14A) RxDx Assay (for Investigational Use Only; VMSI/Roche); [b]by central or local HER2 testing; [c]800 mg/m² at cycle 1 day 1 followed by 600 mg/m² on cycle 1 day 22 and days 1 and 22 of subsequent cycles; [d]at discretion of investigator; [e]800 mg/m² at cycle 1 day 1 followed by 600 mg/m² on day 1 of subsequent cycles; [f]per RECIST version 1.1 by independent review committee; [g]not all secondary endpoints are shown here.

CAPOX, capecitabine + oxaliplatin regimen; CLDN18, claudin 18; CLDN18.2, claudin 18.2; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; 5-FU, 5-fluorouracil; GHS, global health status; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; IV, intravenous; LA, locally advanced; mFOLFOX6, modified folinic acid + fluorouracil + oxaliplatin regimen; mG/GEJ, metastatic gastric or gastroesophageal junction; QoL, quality of life; OG25, Quality of Life of Cancer Patients questionnaire, Oesophago-Gastric Module; ORR, objective response rate; OS, overall survival; PF, physical functioning; PFS, progression-free survival; PRO, patient-reported outcome; Q2W, every 2 weeks; Q3W, every 3 weeks; R, randomized; RECIST, Response Evaluation Criteria in Solid Tumors; TTCD, time to confirmed deterioration.

Figure 2. PFS[a,b] in the Combined Final Analysis[c]

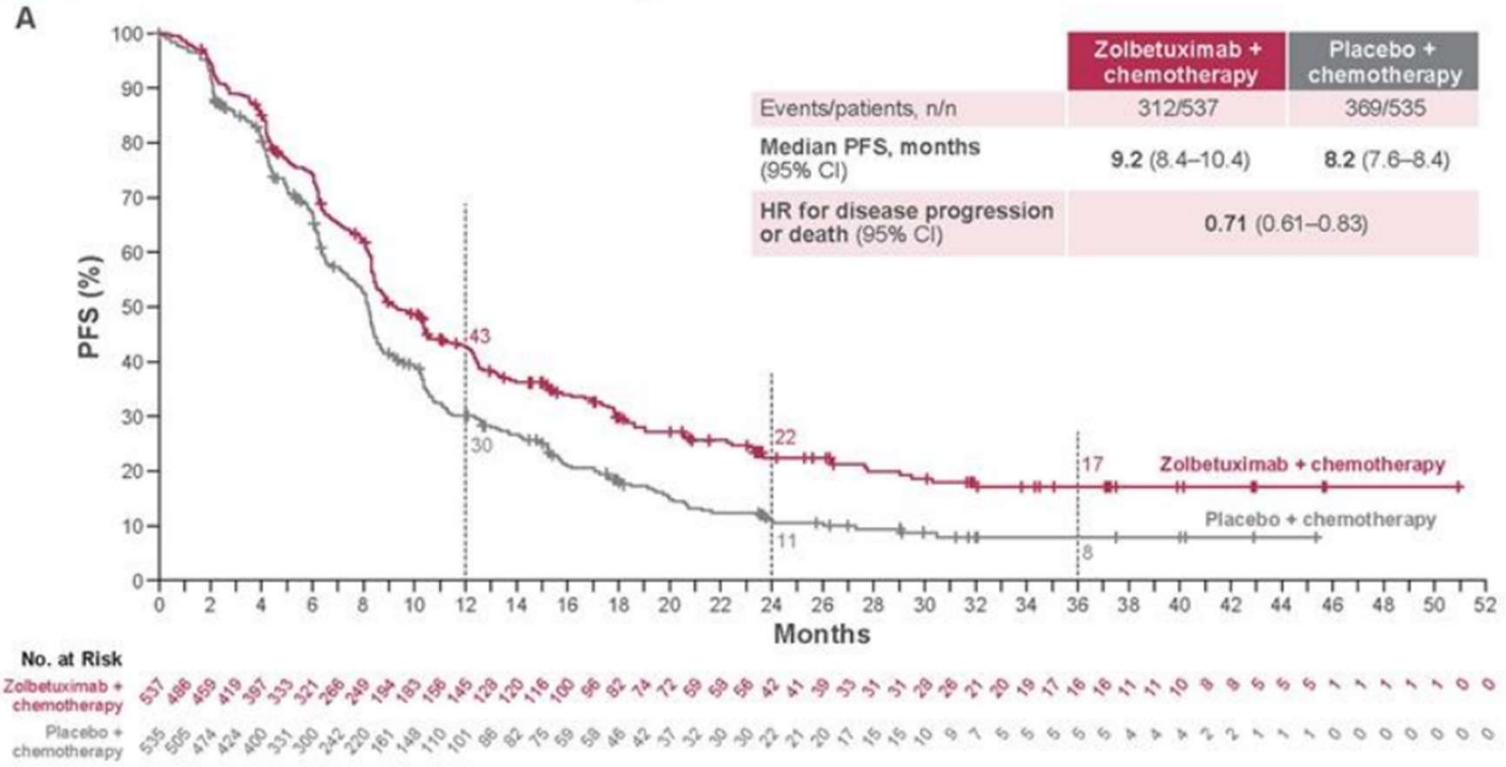


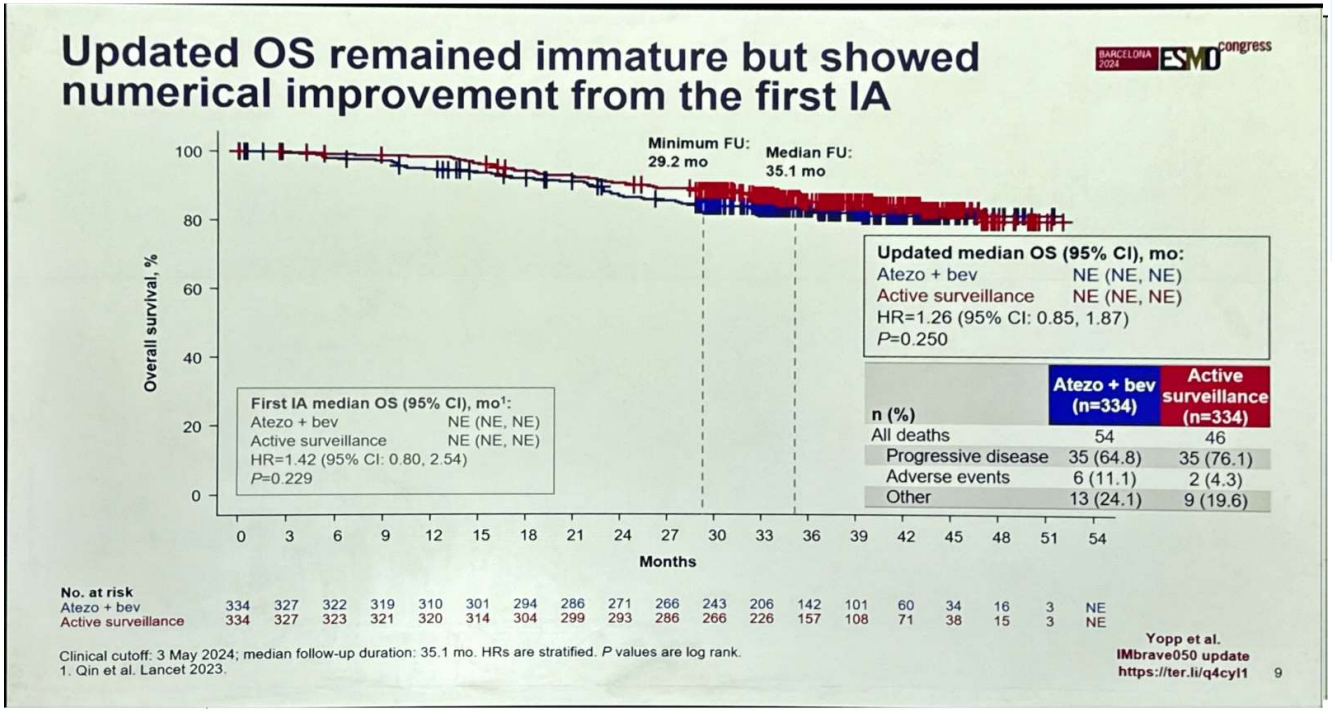
Table 3. Safety Summary in the Combined Safety Analysis Set[a]

Event, n (%)		Zolbetuximab + chemotherapy (n = 533)	Placebo + chemotherapy (n = 527)
TEAEs	All	529 (99.2)	521 (98.9)
	Grade ≥ 3	430 (80.7)	394 (74.8)
	Serious	256 (48.0)	255 (48.4)
TRAEs	Leading to dose interruption of any study drug	385 (72.2)	238 (45.2)
	Leading to dose interruption of zolbetuximab or placebo	286 (53.7)	100 (19.0)
	Leading to discontinuation of any study drug	164 (30.8)	123 (23.3)
	Leading to discontinuation of zolbetuximab or placebo	56 (10.5)	18 (3.4)
	Leading to death	11 (2.1)	12 (2.3)

[a]The safety analysis set comprised all randomly assigned patients who received at least 1 dose of study drug.

TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.

September 2024



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Medicines ▾ Human regulatory ▾ Veterinary regulatory ▾ Committees ▾ News

Home > Medicines > Tecentriq

Tecentriq - withdrawal of application for variation to marketing authorisation

atezolizumab

Medicine post-authorisation | Human

Neoadjuvant immunotherapy in locally advanced MMR-deficient colon cancer

3-year disease-free survival from NICHE-2

M. Chalabi[1], L. van den Dungen, Y. Verschoor, S. Balduzzi, P. de Gooyer, N. Kok, E. Kerver, C. Grootscholten, E. Voest, J. Burger, E. Hendriks, T. de Wijkerslooth, A. Tin, T. Aukema, S. Oosterling, A. Aalbers, J. van den Berg, M. Van Leerdam, T. Schumacher, J. Haanen

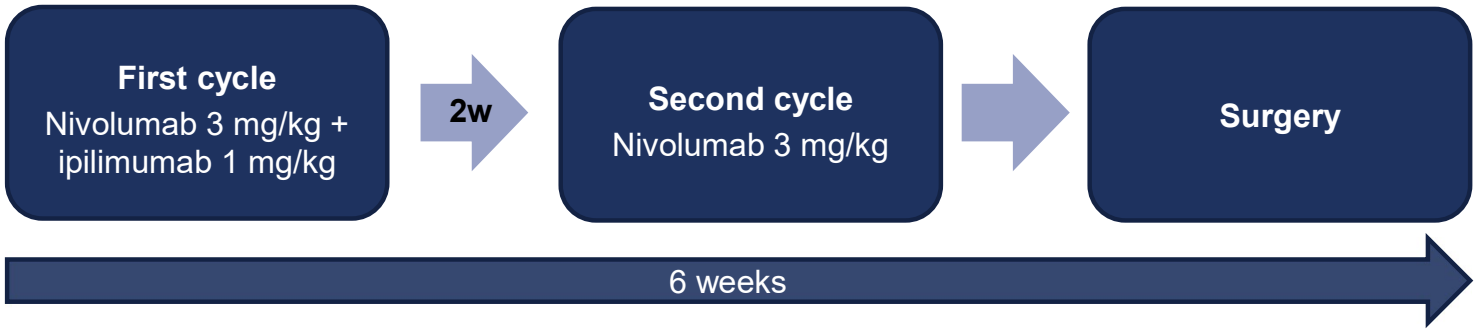
[1]Netherlands Cancer Institute, Amsterdam

NICHE-2 study design

Investigator-initiated, non-randomized multicenter study

Key eligibility criteria

- Non-metastatic dMMR colon cancer, previously untreated
- cT3 and/or N+ based on radiographic staging
- No clinical or radiologic signs of obstruction or perforation
- No active auto-immune disease or use of high dose systemic steroids or immunosuppressive medications

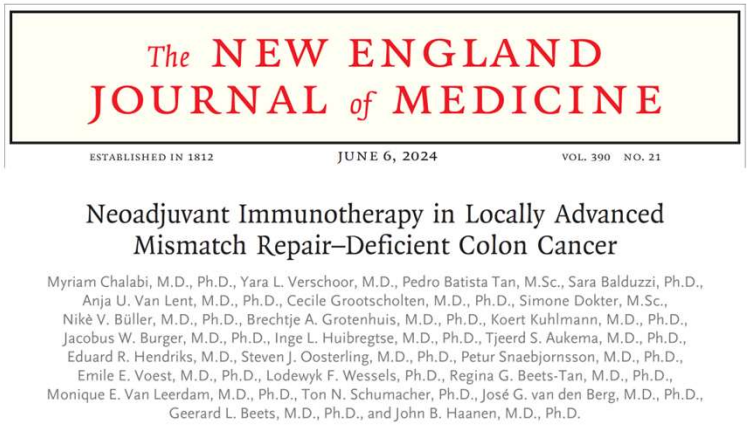


Myriam Chalabi, MD PhD

NICHE-2 safety and pathologic response: recap

- **Safety:** 98% of patients underwent timely surgery meeting the primary safety endpoint
  - No new safety signals

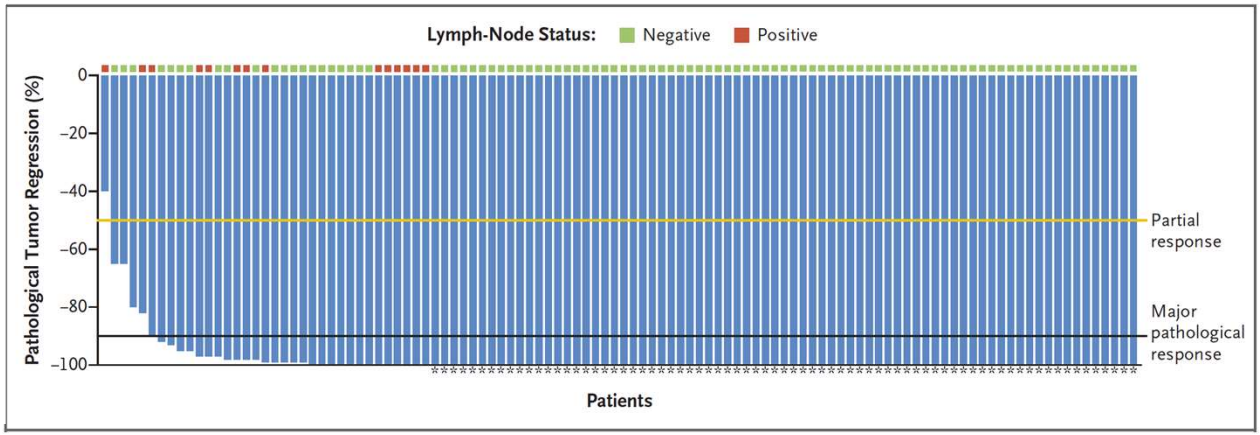
- **Pathologic response** in **98%** of 111 patients in efficacy analysis
  - Major pathologic response (≤10% residual viable tumor) in **95%** of patients
  - Pathologic complete response in **68%** of patients


The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 6, 2024 VOL. 390 NO. 21

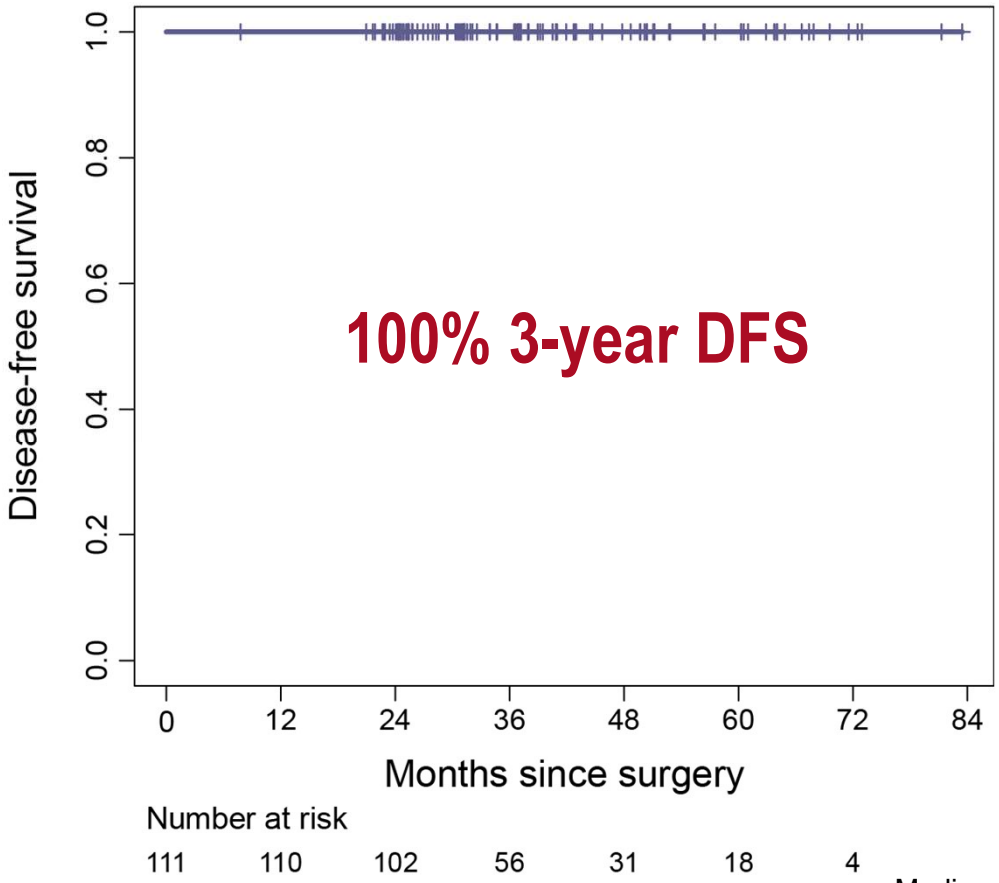
Neoadjuvant Immunotherapy in Locally Advanced Mismatch Repair–Deficient Colon Cancer

Myriam Chalabi, M.D., Ph.D., Yara L. Verschoor, M.D., Pedro Batista Tan, M.Sc., Sara Balduzzi, Ph.D., Anja U. Van Lent, M.D., Ph.D., Cecile Grootscholten, M.D., Ph.D., Simone Dokter, M.Sc., Nikè V. Büller, M.D., Ph.D., Brechtje A. Grotenhuis, M.D., Ph.D., Koert Kuhlmann, M.D., Ph.D., Jacobus W. Burger, M.D., Ph.D., Inge L. Huibregtse, M.D., Ph.D., Tjeerd S. Aukema, M.D., Ph.D., Eduard R. Hendriks, M.D., Steven J. Oosterling, M.D., Ph.D., Petur Snaebjornsson, M.D., Ph.D., Emile E. Voest, M.D., Ph.D., Lodewyk F. Wessels, Ph.D., Regina G. Beets-Tan, M.D., Ph.D., Monique E. Van Leerdam, M.D., Ph.D., Ton N. Schumacher, Ph.D., José G. van den Berg, M.D., Ph.D., Geerard L. Beets, M.D., Ph.D., and John B. Haanen, M.D., Ph.D.



Chalabi et al. NEJM 2024

Results – 3-year disease-free survival 100%



Median follow-up after surgery: 36.5 months (7.8 - 83.4)

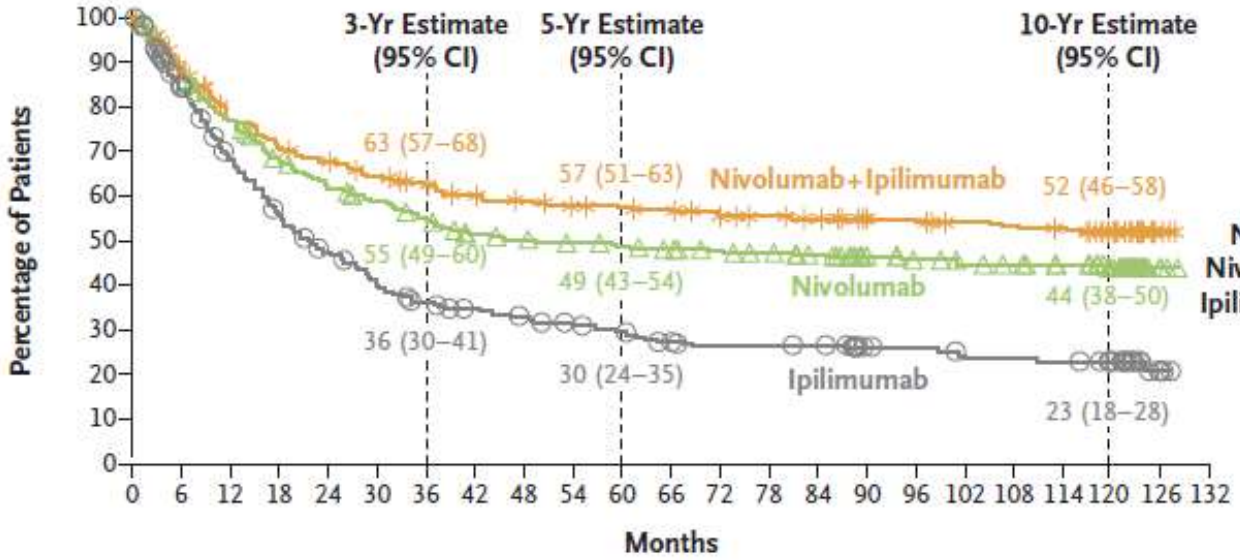
Myriam Chalabi, MD PhD

September 2024

The NEW ENGLAND JOURNAL of MEDICINE

Final, 10-Year Outcomes with Nivolumab plus Ipilimumab in Advanced Melanoma

B Melanoma-Specific Survival



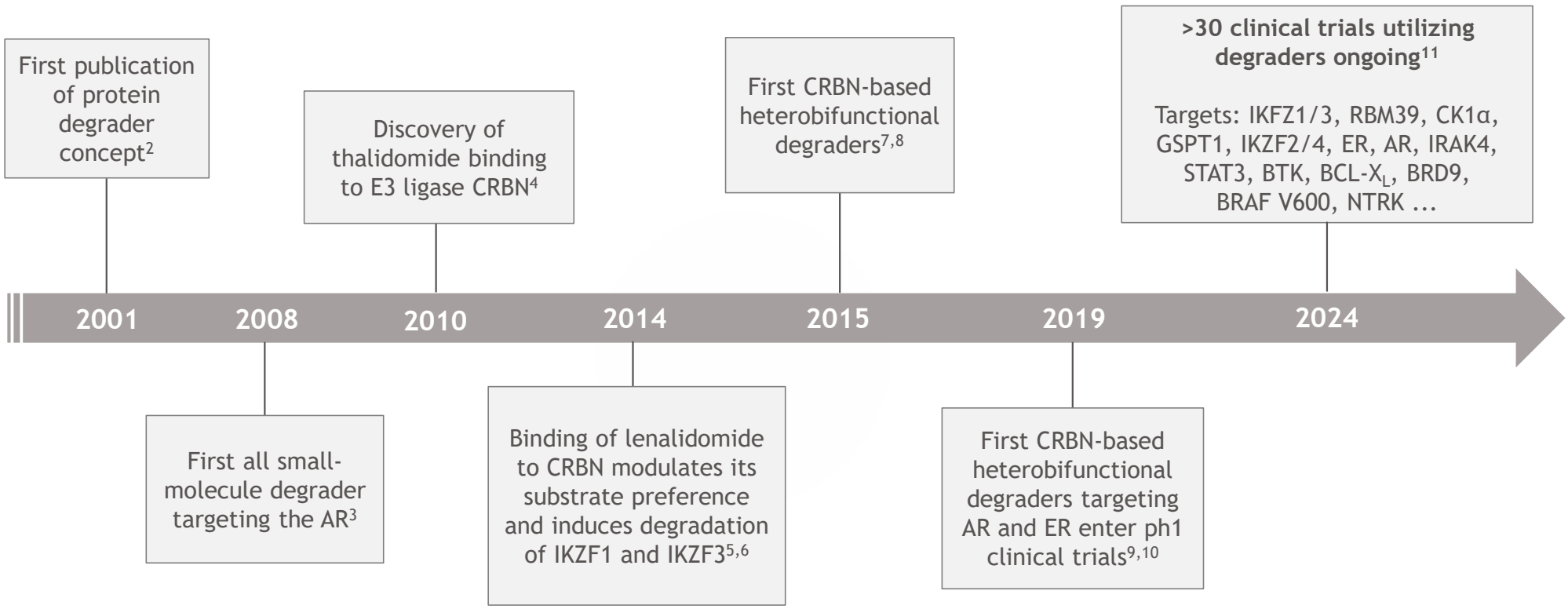
	No. of Patients with Event	Median Melanoma-Specific Survival (95% CI)
		mo
Nivo+Ipi (N=314)	139	NR (71.8–NR)
Nivolumab (N=316)	163	49.4 (35.1–119.4)
Ipilimumab (N=315)	221	21.9 (18.1–27.4)

Hazard ratio for death from melanoma, nivo+ipi vs. ipilimumab, 0.48 (95% CI, 0.39–0.59)
Hazard ratio for death from melanoma, nivolumab vs. ipilimumab, 0.59 (95% CI, 0.49–0.73)
Hazard ratio for death from melanoma, nivo+ipi vs. nivolumab, 0.81 (95% CI, 0.64–1.01)

No. at Risk

Nivo+ipi	314	265	227	210	199	187	179	169	163	158	156	153	147	144	139	126	124	120	117	115	92	10	0
Nivolumab	316	265	231	201	181	171	158	145	141	137	134	130	126	123	118	107	102	98	96	92	77	4	0
Ipilimumab	315	253	203	163	135	113	100	94	87	81	75	68	64	64	63	50	49	44	43	42	35	3	0

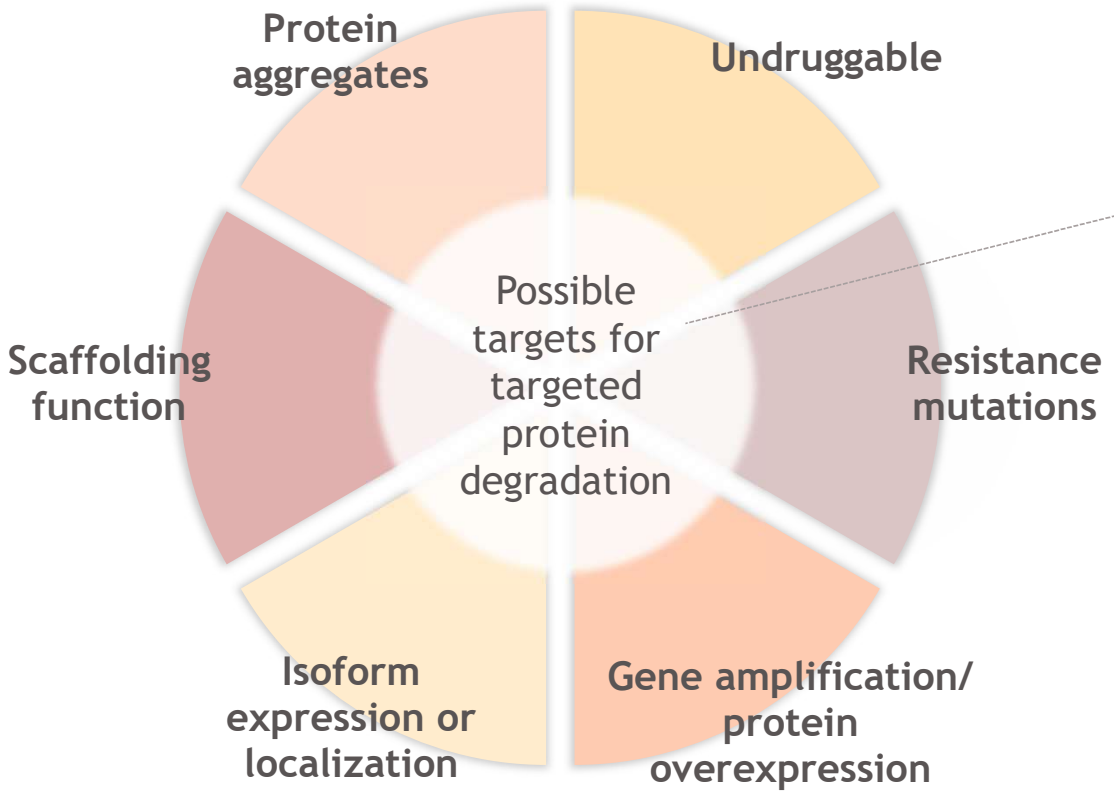
Trends: Targeted protein degradation - Timeline



PROTAC® proteolysis targeting chimera, AR androgen receptor, CRBN cereblon, IMiD immunomodulatory imide drugs, ER estrogen receptor

1. Adapted from: Dale B, et al. Nat Rev Cancer. 2021;21(10):638-654. 2. Sakamoto KM, et al. Proc Natl Acad Sci U S A. 2001;98(15):8554-8559. 3. Schneekloth AR, et al. Bioorg Med Chem Lett. 2008;18(22):5904-5908. 4. Ito T, et al. Science. 2010;327(5971):1345-1350. 5. Krönke J, et al. Science. 2014;343(6168):301-305. 6. Lu G, et al. Science. 2014;343(6168):305-309. 7. Lu J, et al. Chem Biol. 2015;22(6):755-763. 8. Winter GE, et al. Science. 2015;348(6241):1376-1381. 9. ClinicalTrials.gov, National Library of Medicine (US). Identifier NCT04072952. Available from: https://clinicaltrials.gov/study/NCT04072952. 10. ClinicalTrials.gov, National Library of Medicine (US). Identifier NCT03888612. Available from: https://clinicaltrials.gov/study/NCT03888612. 11 Tsai JM, et al. Nat Rev Mol Cell Biol. 2024;25(9):740-757.

Trends: Targeted protein degradation is redifining the druggable space

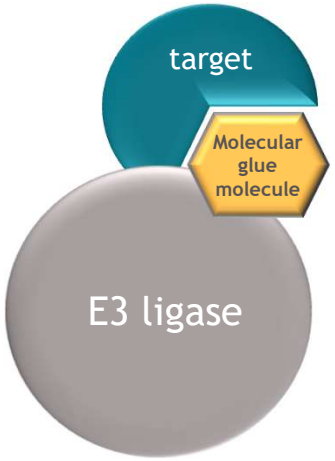


Protein degrader:

- bring the degradation function to the target (event-driven pharmacology)
- negate the need for an active site

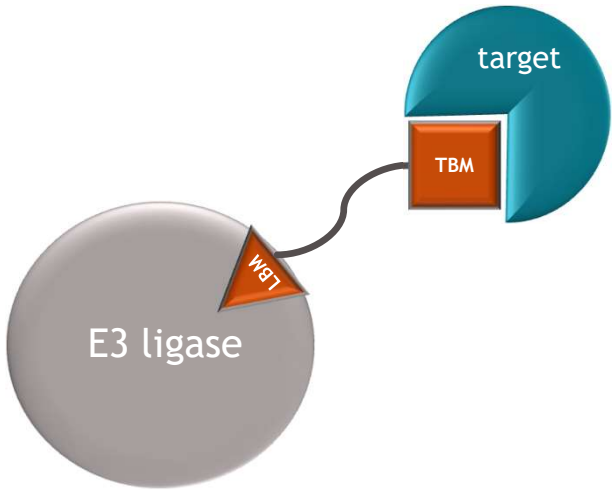
Trends: Targeted protein degradation - Two main modalities

Molecular glue agents
(f.e. IMiDs)



Small molecules that bind to either the ligase or target and **facilitate a neo-interface** between the E3 ubiquitin ligase, the target and the molecular glue[1]

Heterobifunctional degrader
(LDD, PROTAC®)

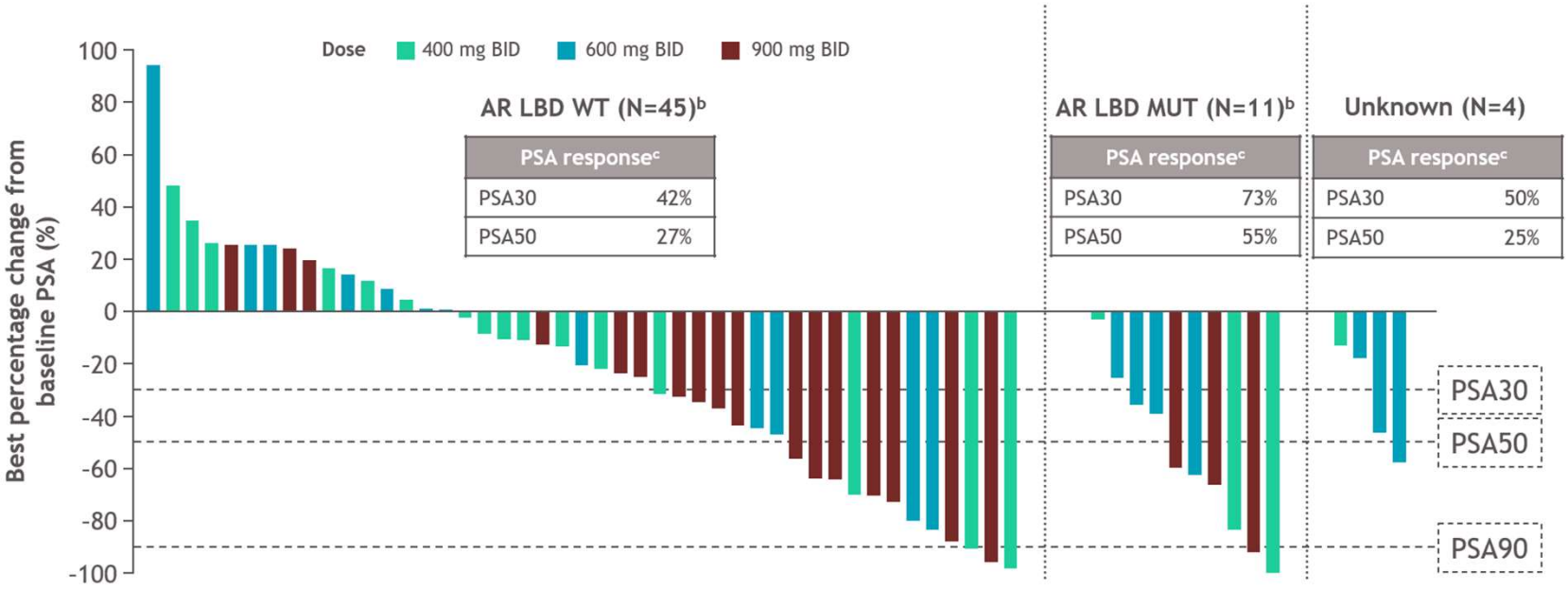


Small molecules containing **separate binding moieties** designed to interact with the E3 ligase and the target **connected by a linker** to induce proximity[1]

IMiD immunomodulatory imide drugs, PROTAC® proteolysis targeting chimera, LBM ligase binding moiety, TBM target binding moiety

1. Tsai JM, et al. Nat Rev Mol Cell Biol. 2024;25(9):740-757.

Trends: Targeted protein degradation - First-in-human phase 1 study design of BMS-986365



AR androgen receptor, mCRPC metastatic castration resistant prostate cancer, ADT androgen deprivation therapy, PC prostate cancer, PSA prostate specific antigen

1. Rathkopf D, et al. ASCO Genitourinary Cancers Symposium; January 25-27, 2024; San Francisco, CA. Abstract 134. Cancer. (Poster)

Zusammenfassung 2024

- <10 IO checkpoint Zulassungen in Bereichen mit hohem medical need
- Next Generation IO checkpoints sind etabliert (LAG-3), keine weiteren checkpoints mit PH3 Daten
- Alternativen in einigen Indikationen (z.B. Lunge, GI) haben deutlich zugenommen
- IO Einsatz schiebt sich in frühere Linien und erstmals von IV zu subkutan


Bristol Myers Squibb™