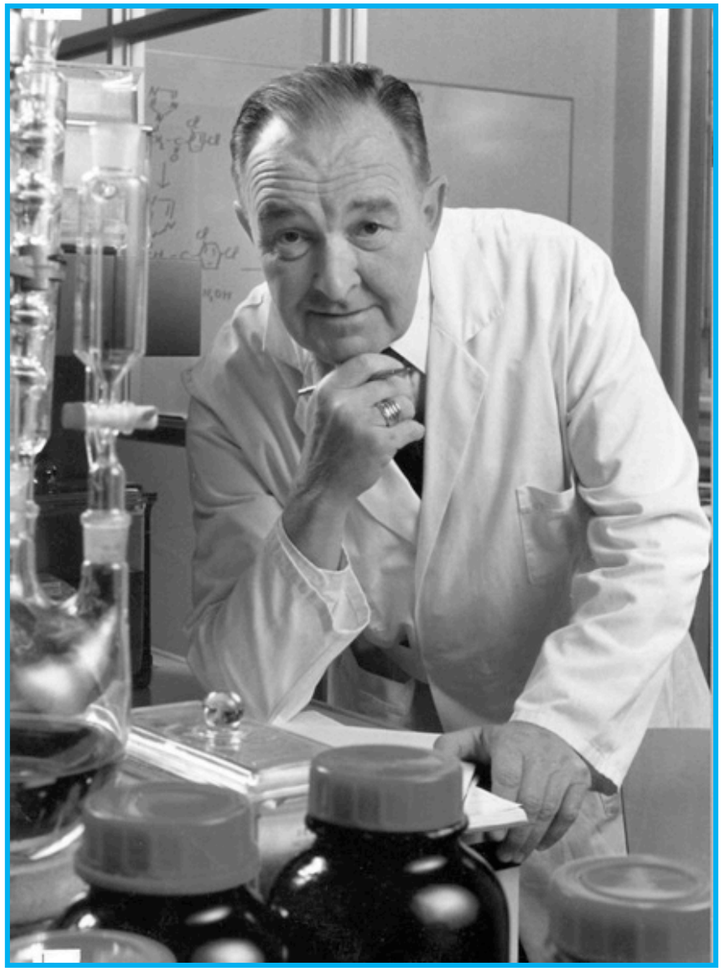
Der Name Janssen…



… geht auf den belgischen Forschergeist und Unternehmensgründer **Dr. Paul Janssen** zurück – einer der **innovativsten und inspirierendsten Wissenschaftler:innen** des 20. Jahrhunderts.

… steht für unser umfassendes Engagement, **nachhaltige Lösungen für Patient:innen und das Gesundheitssystem** durch Fortschritt in Wissenschaft und Medizin zu finden.

"Time is running. Patients are waiting."

Dr. Paul Janssen (1926-2003)

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Janssen Austria

MANAGING DIRECTOR
Ramez Mohsen-Fawzi

GRÜNDUNGSJAHR
1982 als Janssen Pharmaceutica Österreich. Der Standort existiert jedoch bereits seit 1948 unter dem Namen Cilag Österreich.

über 150
Beschäftigte in Österreich

TOP EMPLOYER
2022 wurde Janssen Austria als Teil von Johnson & Johnson zum dritten Mal in Folge als Top Employer ausgezeichnet.

unter den TOP 3
der Pharmaunternehmen in Österreich [1]

13
neue Medikamente im Zeitraum von 2015–Q3 2022

24
Indikationserweiterungen nach jeweilig erfolgter Zulassung im Zeitraum von 2015–Q3 2022

ÖSTERREICHWEITE PARTNERSCHAFTEN

Patient:innen stehen bei allen unseren Tätigkeiten im Mittelpunkt.

Janssen Austria arbeitet deshalb österreichweit mit medizinischem Fach- und Pflegepersonal, Universitäten, Patientenorganisationen und weiteren relevanten Institutionen und Expert:innen im Gesundheitswesen zusammen – denn es sind genau diese Partnerschaften, die dazu führen, Patient:innen neue Perspektiven und innovative Lösungen anbieten zu können.

Wir bei Janssen haben eine Vision: eine Zukunft, in der Krankheiten der Vergangenheit angehören. Wir arbeiten daran, Krankheiten zu bekämpfen, Leben zu verlängern und die Gesundheit zu erhalten.

Janssen-Cilag Pharma GmbH
Vorgartenstraße 206B
A-1020 Wien

AT_CP-307711_v2.0_240ct2022

1. Quelle: IQVIA Gesamtmarkt („TOTA") MAT Aug 2022

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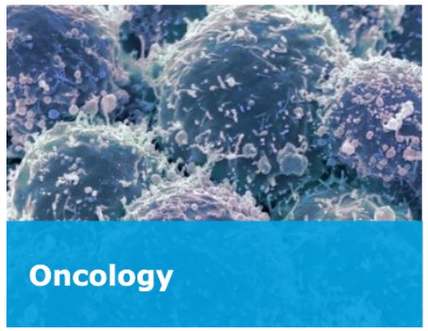
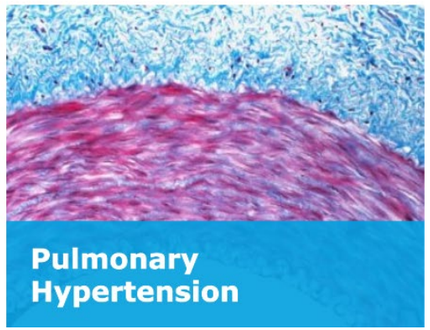
Johnson & Johnson

Unser Ziel:
Verbesserte Versorgung in 6 Therapiegebieten





At Janssen, we're creating a future where disease is a thing of the past.

Vision statement Janssen

Janssen Hämato-Onkologie: Erwartete Zulassungen, Pipeline

Dr. Isabella Eder, Commercial Director Oncology

Jane Kielt, *Mystic Seaport*

A retired art teacher and world traveler, Jane finds painting watercolors healing as she lives through multiple myeloma.

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Janssen Hämatologie/Onkologie 2023

AGENDA

- Janssen Hämato-Onkologie: Überblick
- Daratumumab (MM, AMY): Überblick und klinische Daten
- Cilta-cel (MM): Überblick und klinische Daten
- Teclistamab, Talquetamab (MM): Überblick und klinische Daten
- Solide Tumore: Lung cancer, Prostate cancer & Urothelial cancer

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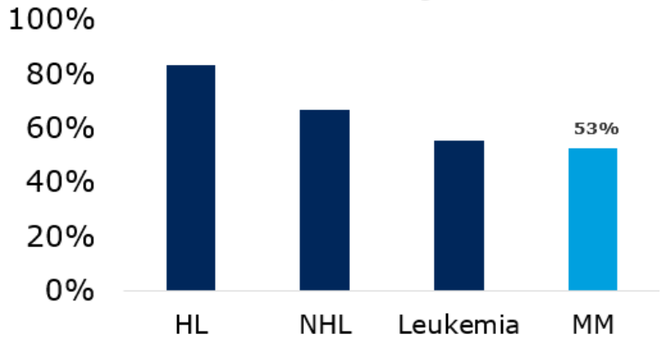
Multiple Myeloma: seltene hämatologische Krebserkrankung, die durch rezidivierende Rückfälle und eine schlechte Prognose gekennzeichnet ist und mit konventionellen Behandlungsmethoden weitgehend unheilbar bleibt.

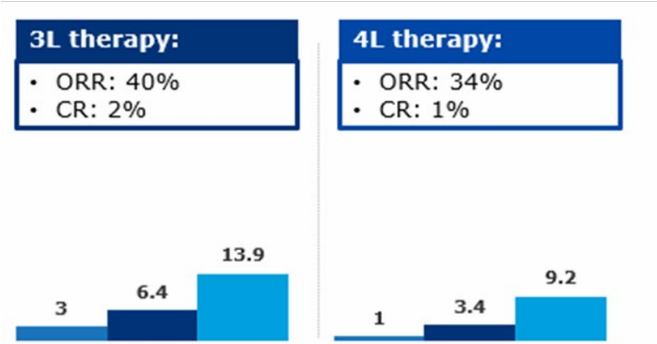
Five-year Survival Rates (UK)[6]

2014-2018, All stages



In addition to having significant morbidities, MM has a 5-year survival rate of only 53% [7]

Outcomes by line of therapy[3-5]



Efficacy of available therapies

Therapy	ORR	Survival (months)
Triplets[6]	31%	11 / 4.8
Selinexor[7,8]	38%	9.3 / 3.7
Belamaf[9]	31%	13.7 / 2.8
Abecma[10]	73%	Not reached / 8.6

Multiple myeloma is an **incurable** disease, with one of the **worst 5-year survival rates** among hematologic cancers (53%), and patients experience **significant clinical morbidities**.

Outcomes worsen with each line of therapy, resulting in minimal, if any, treatment-free intervals and **poor survival** by the time patients become triple-class exposed.

Although triplets are frequently used, there is **no true standard of care** for triple-class exposed patients; **emerging treatments offer little improvement** in efficacy over current options.

3. Verelst 2018; Hemasphere 2(4): e45. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6746001/
4. Gandhi 2019; Leukemia 33(9):2266-2275. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6820050/
5. Yong K, Delforge M, Driessen C, Fink L, Flinois A et al. (2016) Multiple myeloma: patient outcomes in real-world practice. *Br J Haematol* 175 (2): 252-264.
6. Multiple Myeloma Research Foundation – Disease Overview https://themmrf.org/wp-content/uploads/2020/05/MMRF-Disease-Overview.pdf
7. Nuffield Trust & The Health Foundation 2021. Cancer survival rates. https://www.nuffieldtrust.org.uk/resource/cancer-survival-rates

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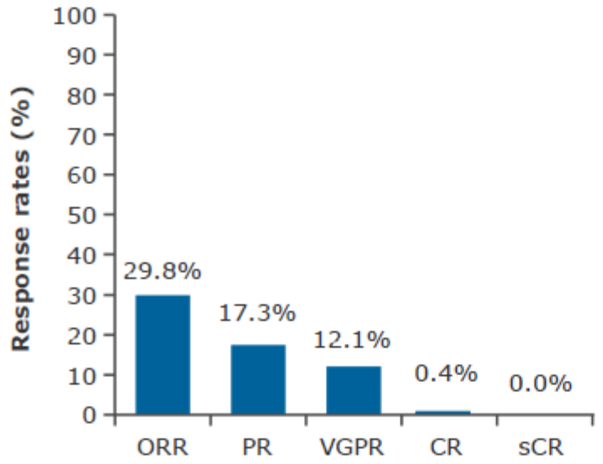
Schlechte Ergebnisse bei Patienten mit RRMM (L3+), die mit PI-, IMiD- und Anti-CD38-Therapien behandelt wurden[1-3]

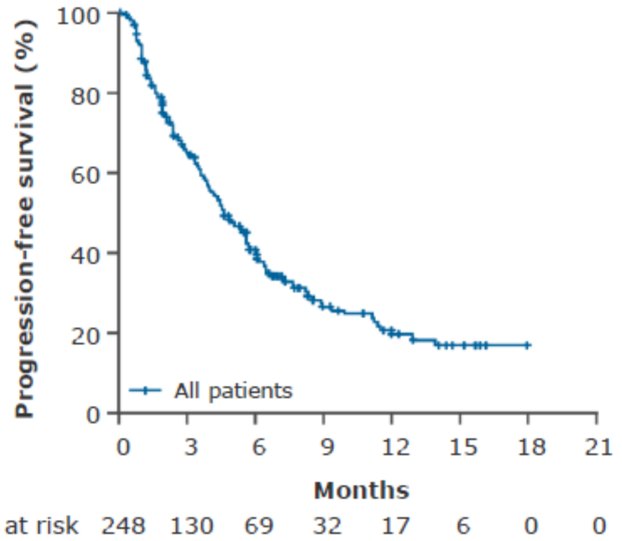
- **LocoMMotion Studie**: United States and 9 European countries[b]
- Patienten erhielten 92 unterschiedliche Therapie-Kombinationen
- Trotz Verfügbarkeit neuer Wirkstoffe im Multiplen Myelom gibt es einen dringenden Bedarf an Behandlungs-alternativen für Patienten, die nach der Einnahme von Anti-CD38, PIs und IMIDs einen Rückfall erleiden.

Depth of response



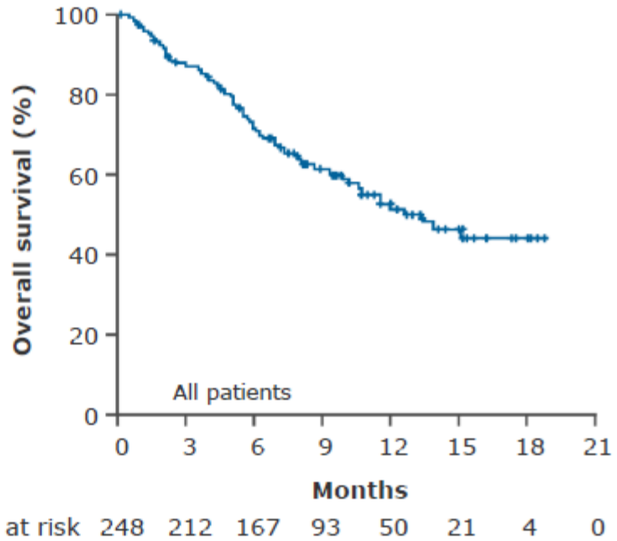
Overall Response Rate : < 30 %

Progression-Free Survival (PFS)



Median PFS: **4.6** months (95% CI 3.9-5.6)

Overall Survival* (OS)



Median OS: **12.4** months (95% CI 10.28-NE)

[b]Belgium, France, Germany, Italy, Netherlands, Poland, Russia, Spain and United Kingdom

NE, not estimable. MM, Multiple Myeloma, CR, complete response; mOS, median overall survival; ORR, overall response rate; OS, overall survival; SoC, standard of care; TTNT, time to next treatment; VGPR, very good partial response;

1. Mateos MV *et al.* Poster presented at: Virtual ASCO Annual Meeting; 4–8 June 2021. 2. Haefliger B *et al.* Poster presented at: EHA-EBMT 3rd CAR T-cell Virtual Meeting; 4–6 February 2021. 3.Moreau et al. ASH 2021, abstract 3057 (poster presentation)

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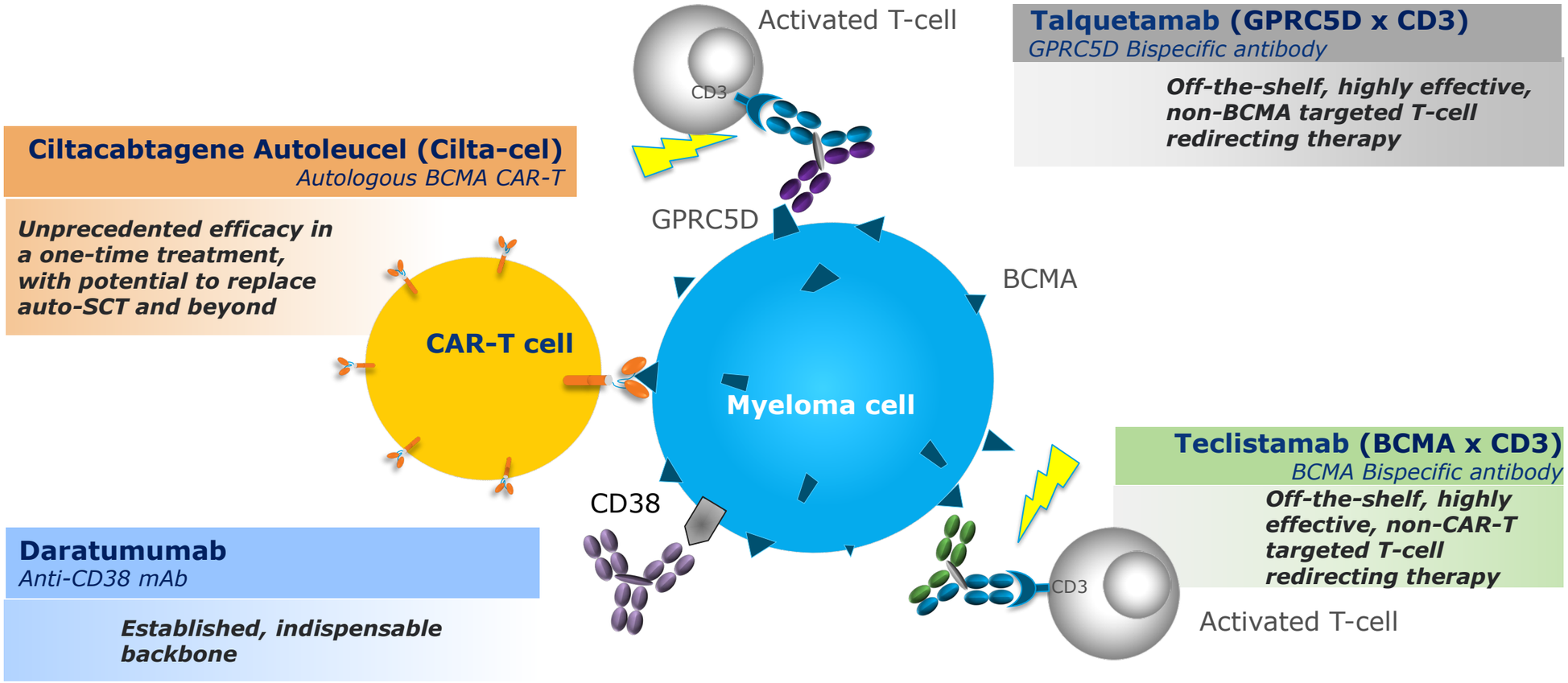
Unser Commitment/Portfolio um PatientInnen mit MM zu heilen



Talquetamab (GPRC5D x CD3)
GPRC5D Bispecific antibody

Off-the-shelf, highly effective, non-BCMA targeted T-cell redirecting therapy

Ciltacabtagene Autoleucel (Cilta-cel)
Autologous BCMA CAR-T

Unprecedented efficacy in a one-time treatment, with potential to replace auto-SCT and beyond

Teclistamab (BCMA x CD3)
BCMA Bispecific antibody

Off-the-shelf, highly effective, non-CAR-T targeted T-cell redirecting therapy

Daratumumab
Anti-CD38 mAb

Established, indispensable backbone

Build curative regimens: Different targets with ***transformative efficacy***, that are ***complementary***, ***combinable***, and create options for ***tailored regimens***

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DARZALEX

Anti CD-38 Antikörper

Skin cells at 20x magnification

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Darzalex: aktueller Stand der Zulassungen

	Zulassungsdatum	Zulassungsstudie und Erstpublikation	Vergleichs-therapie
1. Linie Multiples Myelom			
Transplant Ungeeignet Darzalex + Velcade + Melphalan + Prednison (D-VMP)	August 2018	ALCYONE (NCT02195479) Mateos et al., N Engl J Med 2018;378:518-28.	VMP
Transplant Ungeeignet Darzalex + Revlimid + Dexamethason (D-Rd)	November 2019	MAIA (NCT02252172) Facon et al., N Engl J Med 2019;380:2104-15.	Rd
Transplant geeignet Darzalex + Velcade + Thalidomid + Dexamethason (D-VTd)	Jänner 2020	CASSIOPEIA (NCT02541383) Moreau et al., Lancet 2019; 394: 29–38	VTd
≥ 2 Linien Multiples Myelom			
Darzalex + Revlimid + Dexamethason (D-Rd)	Mai 2017	POLLUX (NCT02076009) Dimopoulos et al., N Engl J Med 2016;375:1319-31.	Rd
Darzalex + Vecade + Dexamethason (D-Vd)	Mai 2017	CASTOR (NCT02136134) Palumbo et al., N Engl J Med 2016;375:754-66.	Vd
Darzalex + Carfilzomib + Dexamethason (K-Dd, AMGEN) Darzalex + Pomalidomid + Dexamethason (D-Pd)	Dezember 2020 Juli 2021	CANDOR (NCT03158688), Zulassung durch AMGEN geführt Dimopoulos et al., Lancet 2020; 396: 186–97 APOLLO (NCT03180736)	Kd Pd
≥ 3 Linien Multiples Myelom			
Darzalex Monotherapie	Mai 2016	GEN-501 SIRIUS	n.a.
Alle Linien Multiples Myelom			
Subkutane Verabreichung	Juni 2020	COLUMBA (NCT03277105) Mateos et al., Lancet Haematol. 2020 May;7(5):e370-e380.	i.v.
Split-Dose (1. Infusion: 2x 8mg/kg, statt 1x 16mg/kg)	Jänner 2019	EQUULEUS (NCT01998971)	n.a.
1. Linie AL-Amyloidose			
Darzalex + Cyclophosphamid + Velcade + Dexamethason (D-VCd)	Juli - 2021	ANDROMEDA (NCT03201965)	VCd

Darzalex: Erwartete Zulassungen 2024+

Produkt/Indikation	Zulassungsdatum	Zulassungsstudie	Vergleichstherapie
1. Linie Smouldering Myeloma			
Darzalex Monotherapie	Q1 - 2026	AQUILA (NCT03301220)	Active Monitoring
1. Linie Multiples Myelom			
Transplant Geeignet Darzalex + Velcade + Revlimid + Dexamethason (D-VRd)	Dec - 2024	PERSEUS (NCT03710603)	VRd
1. Linie Multiples Myelom Smouldering Myeloma			
Transplant Ungeeignet Darzalex + Velcade + Revlimid + Dexamethason (D-VRd)	Q2 - 2027	CEPHEUS (NCT03652064)	VRd

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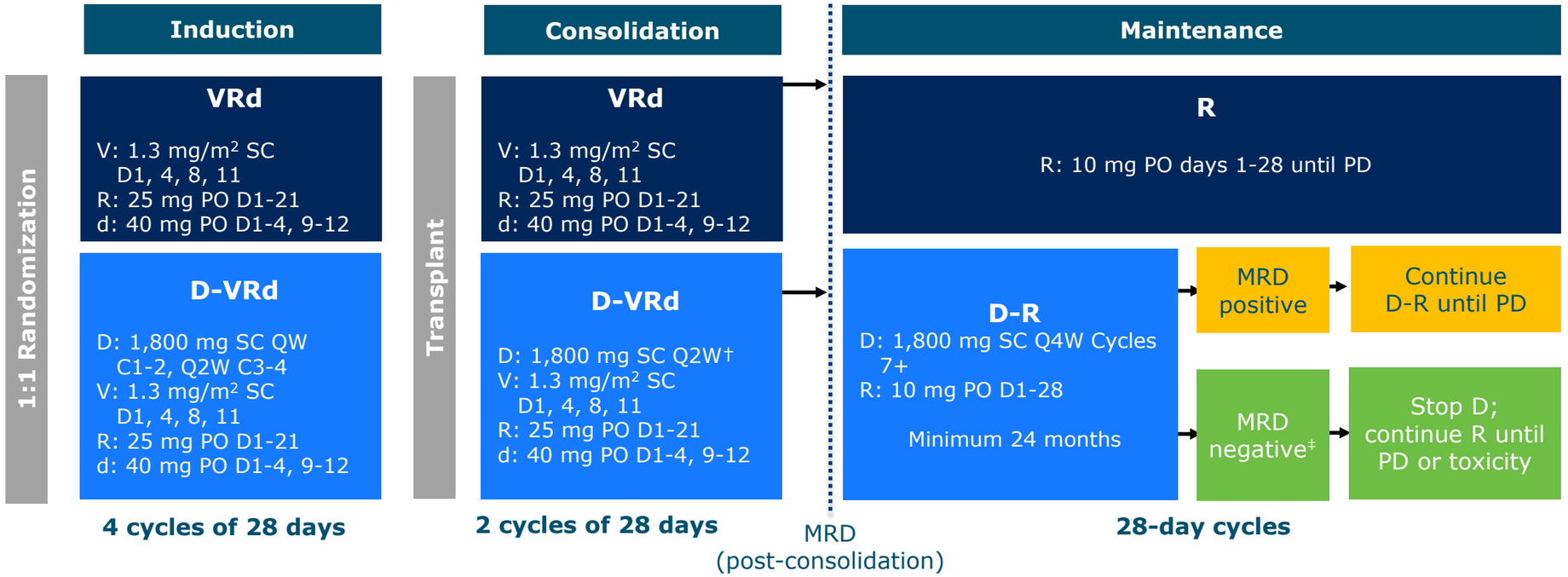
PERSEUS: A Phase 3 Study Comparing D-VRd vs VRd in Transplant-Eligible Patients With Newly Diagnosed Multiple Myeloma*

Phase 3, Randomized, Multicenter Study

Patients:

- Transplant-eligible NDMM
- Aged 18-70 years
- ECOG PS ≤2
- N=690



†Patients with a post-ASCT recovery period >12 weeks off DARA SC should restart DARA SC Q2W for 2 cycles, then Q4W thereafter.
‡If ≥1 year of sustained MRD negativity, restart DARA SC (QW for 8 weeks, Q2W for 16 weeks, Q4W thereafter) at the time of loss of MRD negativity or relapse from CR.

Primary Outcome:	Secondary Outcomes:	
• Progression-free survival	• Minimal residual disease • Overall response rate	• PFS2 • Overall survival

*Ex-US study.
ASCT, autologous stem cell transplant; C, cycle; CR, complete response; D, daratumumab; d, dexamethasone; D#, day; MM, multiple myeloma; PFS2, progression-free survival on the next line of therapy; PD, progressive disease; QW, every week; Q2W, every 2 weeks; R, lenalidomide; SC, subcutaneous; V, bortezomib.
Sonneveld et al. Poster presented at: ASCO 2019. Abstract TPS8055. NCT03710603 www.clinicaltrials.gov.

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Carvykti®
(Ciltacabtagene-autoleucel)

BCMA-targeted autologous CAR-T cell therapy for Multiple Myeloma (MM)

Michaela Boczek, MBA – Cell Therapy Lead Austria

Skin cells at 20x magnification

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CARVYKTI® ist eine innovative Therapieoption, die Multiplen Myelom-Patienten das Potenzial für eine einmalige Behandlung und eine dauerhafte Krankheitsremission bietet.[1-8]

Erstzulassungen 2022

Produkt/Indikation	Zulassungsdatum	Zulassungsstudie	Vergleichstherapie
4. Linie Multiples Myelom			
CARVYKTI® (Ciltacabtagene-autoleucel)	25. Mai 2022	CARTITUDE-1 NCT03548207[8]	Phase 1b/2, multi-center registration study of **single arm** JNJ-4528 in RRMM

CARVYKTI ist indiziert für die Behandlung erwachsener Patienten mit rezidiviertem und refraktärem multiplen Myelom, die zuvor bereits mindestens drei Therapien erhalten haben, darunter einen Immunmodulator, einen Proteasom-Inhibitor sowie einen anti-CD38-Antikörper, und die während der letzten Therapie eine Krankheitsprogression zeigten.

Weitere Zulassungen 2024 - 2026

Produkt/Indikation	Zulassungsdatum	Zulassungsstudie	Vergleichstherapie
≥ 1.-3. Linie Multiples Myelom			
CARVYKTI® (Ciltacabtagene-autoleucel)	Q1-2024	CARTITUDE-4 NCT04181827[9]	Phase 3 study comparing efficacy of JNJ-4528 with standard therapy (**PVd or DPd)**
Frontline TIE Multiples Myelom			
CARVYKTI® (Ciltacabtagene-autoleucel)	~Q1-2026	CARTITUDE-5 NCT04181827[10]	Phase 3 Study of **Cilta-cel vs VRd → Rd** in Transplant Non-Intended NDMM

References:
1. EMA. List of medicines currently in PRIME scheme. 2019. Available at https://www.ema.europa.eu/documents/report/list-products-granted-eligibility-prime_en-0.xlsx; **2.** EMA. Advanced therapy medicinal products https://www.ema.europa.eu/en/human-regulatory/overview/advanced-therapy-medicinal-products-overview; **3.** Locke et al. The Lancet. Oncology. 2019 Jan;20(1):31-42; **4.** Maude et al. The New England journal of medicine. 2018 Feb 1;378(5):439-48; **5.** EMA. First two CAR-T cell medicines recommended for approval in the European Union. 2018. Available at https://www.ema.europa.eu/en/news/first-two-car-t-cell-medicines-recommended-approval-european-union; **6.** Pasquini et al. Abstract 764. Presented at 61st ASH Annual Meeting December 7-10 Orlando, Florida. 2019; **7.** Grupp et al. Abstract 2619. Presented at 61st ASH Annual Meeting December 7-10 Orlando, Florida. 2019; **8.** Jaglowski et al. Abstract 766. Presented at 61st ASH Annual Meeting December 7-10 Orlando, Florida. 2019. **9.** CARTITUDE-1: NCT03548207. Available: https://clinicaltrials.gov/ct2/show/NCT03548207.; **9.** CARTITUDE-4: NCT04181827. Available: https://clinicaltrials.gov/ct2/show/NCT04181827. **10.**CARTITUDE-5 NCT04923893. Available: https://clinicaltrials.gov/ct2/show/NCT04923893 ; **11.** CARVYKTI Fachinformation Stand März 2023; TIE: Transplant ineligible

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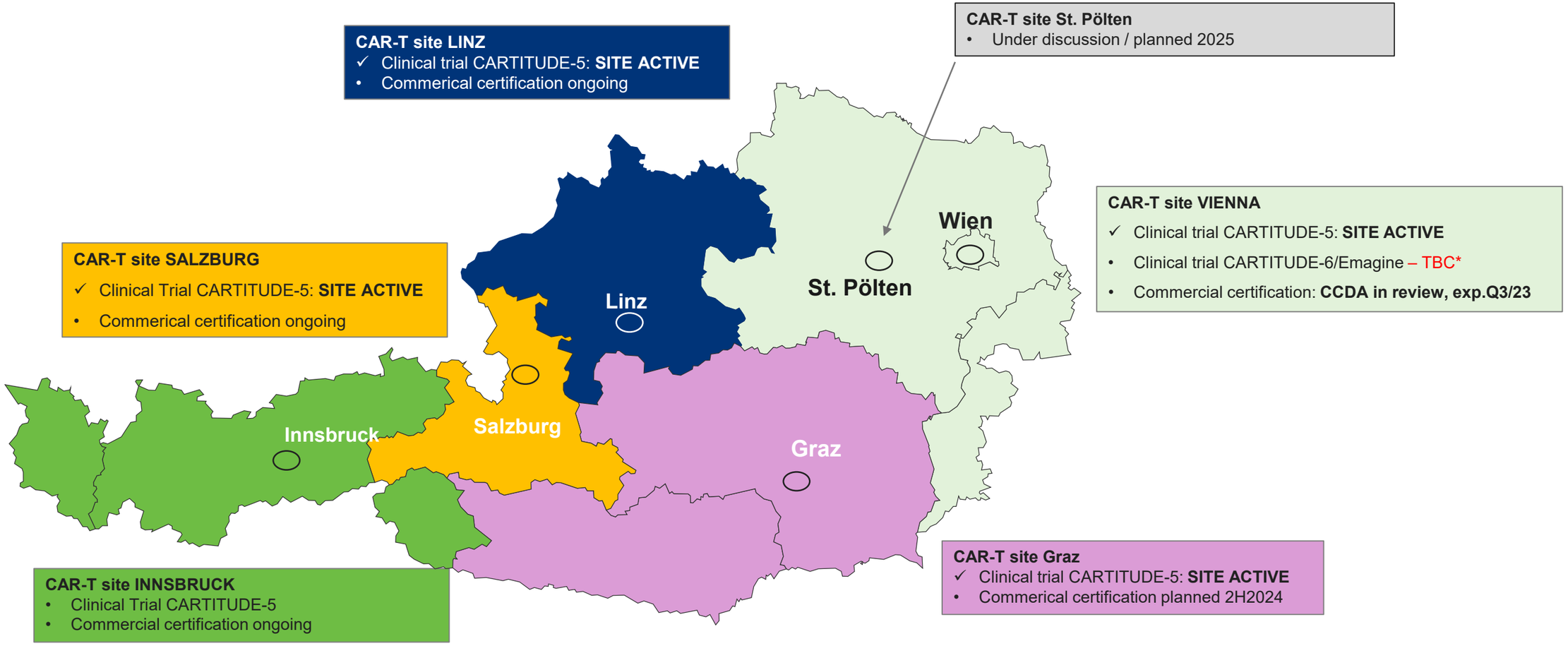
Österreich gehört zu den ersten beiden Ländern, die CARVYKTI® in der EMEA-Region einführen (Verfügbarkeit ab April‘24).

Die Verfügbarkeit ist noch bis Ende 2024 stark limitiert. Zwischenzeitlich wurden die CAR-T-Standorte für die Teilnahme am CARTITUDE-Studienprogramm aktiviert.



References:

CARTITUDE-5: Phase 3 study comparing efficacy of VRd + Cilta-Cel vs. VRd+Rd in a frontline setting (NDMM)

CARTITUDE-6: Phase 3 study comparing efficacy of DVRD+ Cilta-Cel vs. DVRD+ ASCT (NDMM)

*TBC – to be confirmed by European Myeloma Network

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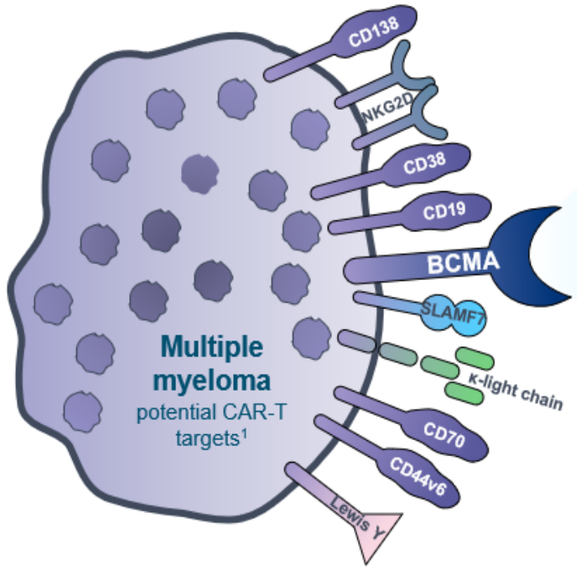
CARVYKTI® Wirkmechanismus[1]

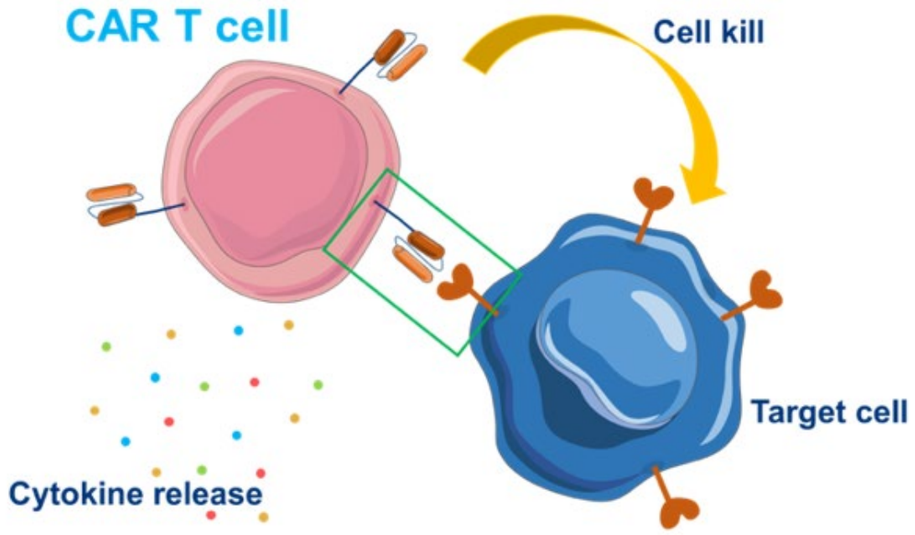
Cilta-cel ist ein auf genetisch veränderten autologen Zellen basierendes Arzneimittel, das T-Zellen enthält, welche ex vivo mit einem replikationsinkompetenten lentiviralen Vektor transduziert wurden, der für einen chimären Antigenrezeptor (CAR) gegen das B-ZellReifungsantigen (BCMA) kodiert.[1]

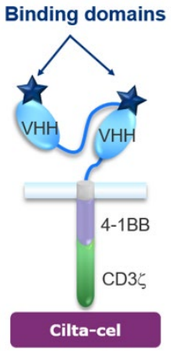
BCMA in Multiple Myeloma



- Essential for the survival of long-lived bone marrow plasma cells[2]
- Most other cells do not express BCMA[2,3]
- Highly expressed on MM cells[2]

Expression profile makes BCMA a good candidate for CAR-T therapy[1,3–5]





1 CARVYKTI Fachinformation. Stand März 2023

BCMA=B-cell maturation antigen; CAR-T=chimeric antigen receptor-T cell; CD=cluster of differentiation; MM=multiple myeloma; NKG2D=natural killer group 2D; SLAMF7=signaling lymphocytic activation molecule family member 7.

1. D'Agostino M, et al. Curr Hematol Malig Rep. 2017;12(4):344–57. / 2. O'Connor BP, et al. J Exp Med. 2004;199(1):91–8.; 3. Friedman KM, et al. Hum Gene Ther. 2018;29(5):585–601. / 4. Tai YT, Anderson KC. Immunotherapy. 2015;7(11):1187–99.; 5. Seckinger A, et al. Cancer Cell. 2017;31(3):396–410.; *Adapted from BerdejaJG, MadduriD, UsmaniSZ, et al. Oral presentation presented at: The Annual American Society of Clinical Oncology (ASCO) Virtual Scientific Program; May 29-31, 2020.

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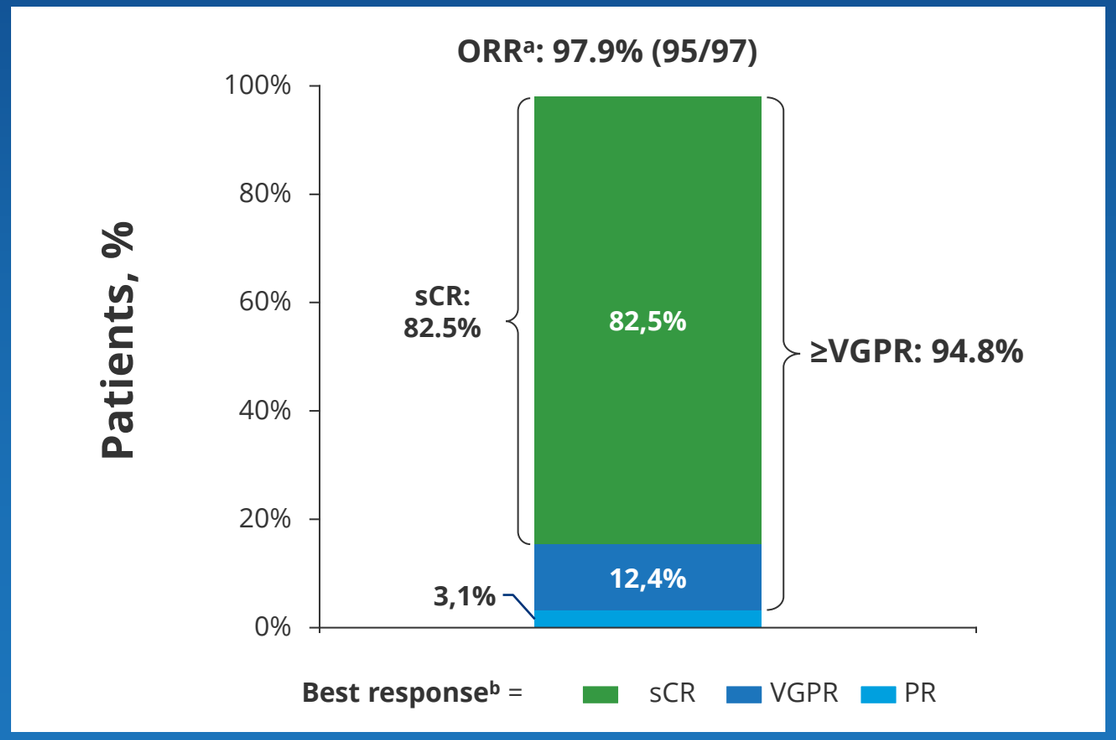
Lin Y, et al. ASCO 2023. Poster 8009

CARTITUDE-1 Final Results
(~3-Year Follow-Up)

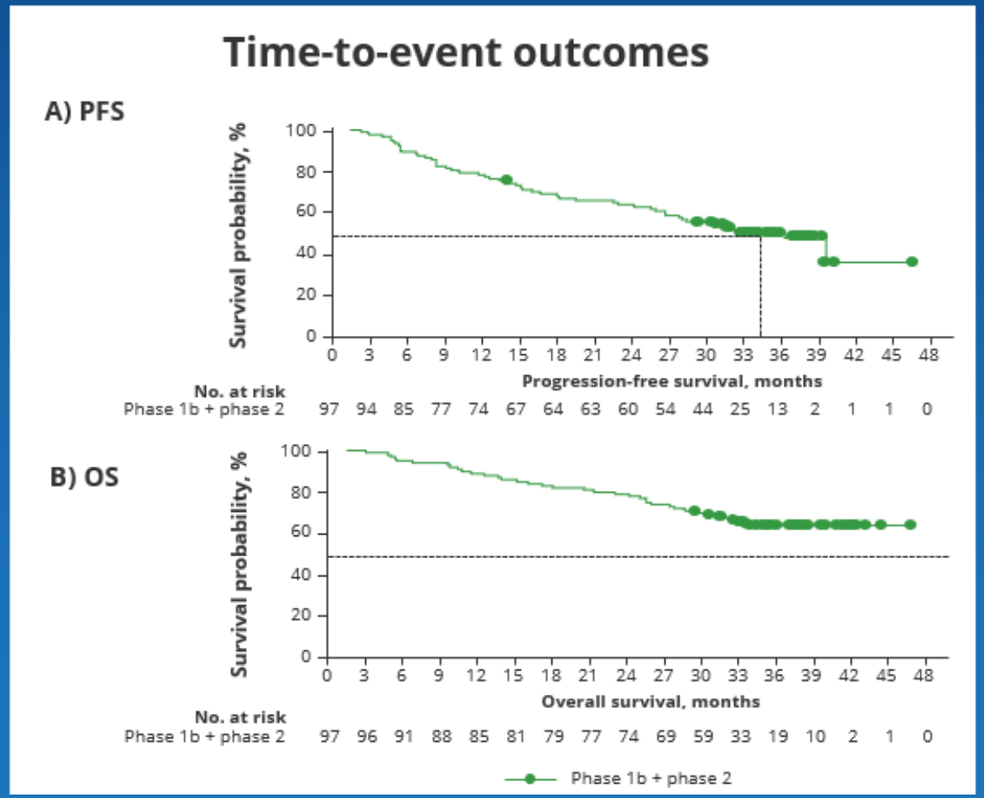
Previously reported primary endpoint

- ORR as assessed by independent review committee was 97.9% (95% CI, 92.7–99.7)[1]
  - 82.5% (95% CI, 73.4–89.4) achieved sCR[1]



At study closeout:

- Median DOR was 33.9 months (95% CI, 25.5–NE)
- Median PFS was 34.9 months (95% CI, 25.2–NE)
- Median OS was not reached
  - An estimated 62.9% of patients were alive at ~3-year follow-up



[a]ORR assessed by independent review committee. [b]No patient had CR or stable disease. CR, complete response; ORR, overall response rate; PR, partial response; sCR, stringent complete response; VGPR, very good partial response. 1. Martin T, et al. *J Clin Oncol* 2023;41:1265-74. DOR, duration of response; NE, not estimable; OS, overall survival; PFS, progression-free survival.

Safety of Cilta-cel based on CARTITUDE 1

	N=97	
	Any grade	Grade 3/4
Hematologic AEs ≥25%, n (%)		
Neutropenia	93 (95.9)	92 (94.8)
Anemia	79 (81.4)	66 (68.0)
Thrombocytopenia	77 (79.4)	58 (59.8)
Leukopenia	60 (61.9)	59 (60.8)
Lymphopenia	51 (52.6)	48 (49.5)
Nonhematologic AEs ≥25%, n (%)		
Metabolism and nutrition disorders		
Hypocalcemia	31 (32.0)	3 (3.1)
Hypophosphatemia	30 (30.9)	7 (7.2)
Decreased appetite	28 (28.9)	1 (1.0)
Hypoalbuminemia	27 (27.8)	1 (1.0)
Gastrointestinal		
Diarrhea	29 (29.9)	1 (1.0)
Nausea	27 (27.8)	1 (1.0)
Other		
Fatigue	36 (37.1)	5 (5.2)
Cough	34 (35.1)	0
AST increased	28 (28.9)	5 (5.2)
ALT increased	24 (24.7)	3 (3.1)

CRS	**N=97**
Patients with a CRS event,[a] n (%)	92 (94.8)
Time to onset, median (range) days	7 (1–12)
Duration, median (range) days	4 (1–97)[b]

Of 92 patients with CRS, majority (94.6%) were grades 1/2
CRS resolved in 91 (98.9%) patients within 14 days of onset

	N=97
Total CAR T-cell neurotoxicities, n (%)	
Any Grade	20 (20.6)
Grade ≥3	10 (10.3)
ICANS, n (%)	
Any Grade	16 (16.5)
Grade ≥3	2 (2.1)
Other neurotoxicities,[c] n (%)	
Any Grade	12 (12.4)
Grade ≥3	9 (9.3)

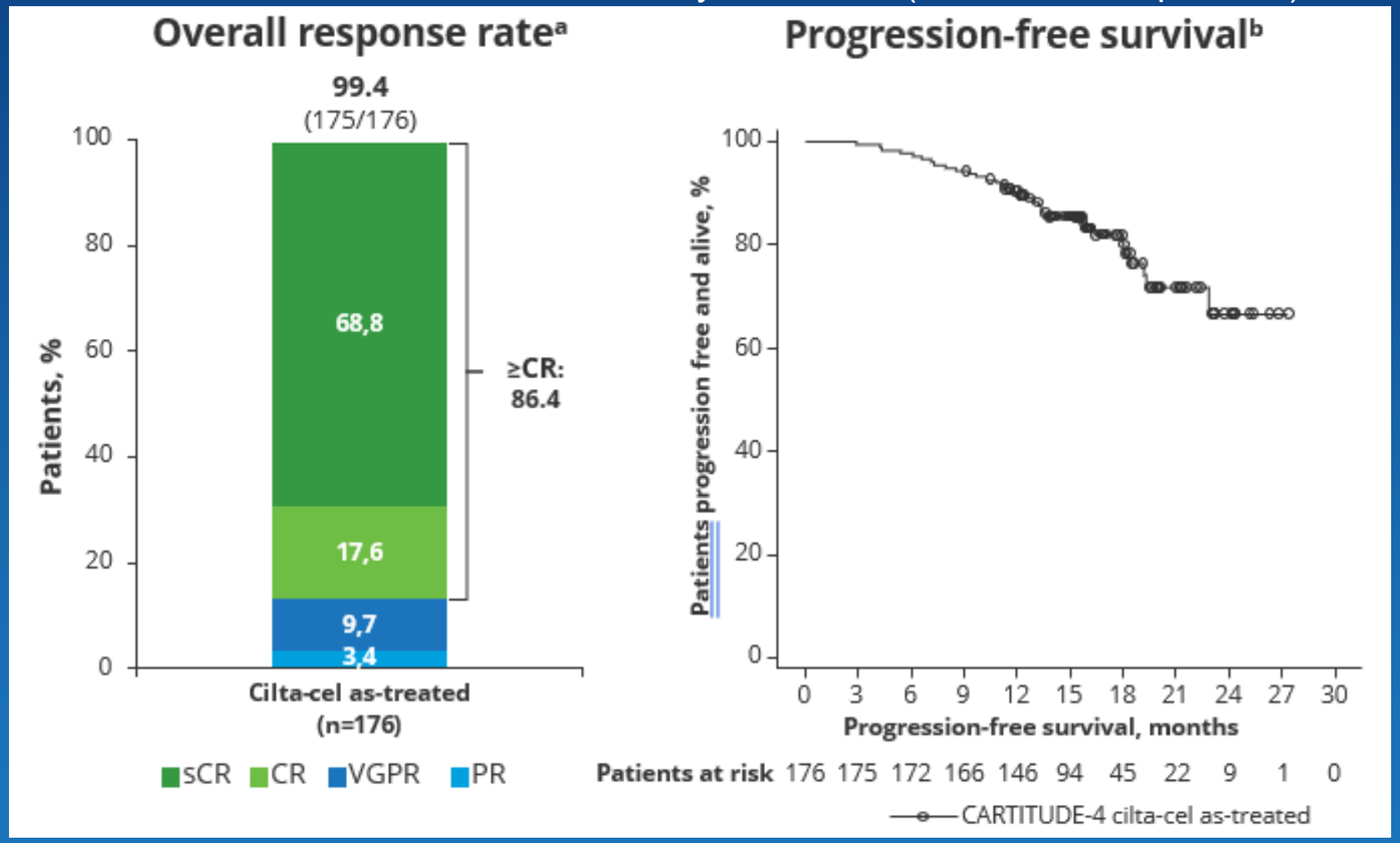
[a]CRS was graded using Lee et al. (Blood 2014) in the phase 1b portion of the study and ASTCT in phase 2; in this combined analysis, Lee et al. criteria were mapped to ASTCT criteria for patients in the phase 1b portion. [b]The patient with 97-day duration died due to CRS/HLH. [c]Events not reported as ICANS (ie, onset after a period of recovery from CRS and/or ICANS).
AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ASTCT, American Society for Transplantation and Cellular Therapy; CRS, cytokine release syndrome; HLH, hemophagocytic lymphohistiocytosis.

1. Usmani S et al. ASCO2021. Abstract 8005

CARTITUDE-4: mFU 15,9 Months - FIRST RESULTS

Phase 3 study comparing cilta-cel vs physicians' choice of either DPd or PVd in patients with lenalidomide-refractory MM after 1–3 prior LOT2

Patients Treated With Cilta-cel as Study Treatment (As-Treated Population)



- This represents a patient population with clear unmet need commonly seen in clinical practice
- Median follow-up was 15.9 months
- For the as-treated population (n=176):
  - 99% ORR, with 86% ≥CR
  - 72% MRD negative at 10^{-5} (n=126/176)
  - 90% PFS rate (from apheresis) at 12 months

[a]Assessed using a validated computerized algorithm; ORR is defined as the proportion of subjects who achieve a PR or better per IMWG criteria. [b]Baseline begins at apheresis and excludes patients randomized to cilta-cel who had disease progression during bridging therapy or lymphodepletion, or died, and thus were not eligible to receive cilta-cel as study treatment.

cilta-cel, ciltacabtagene autoleucel; CR, complete response; IMWG, International Myeloma Working Group; ORR, overall response rate; PFS, progression-free survival; PR, partial response; sCR, stringent complete response; SOC standard of care; VGPR, very good partial response.

CARTITUDE-4: mFU 15,9 Months - FIRST RESULTS

Primary Endpoint – PFS (ITT Population), Secondary Endpoints – MRD and OS

PFS: Cilta-cel vs SOC

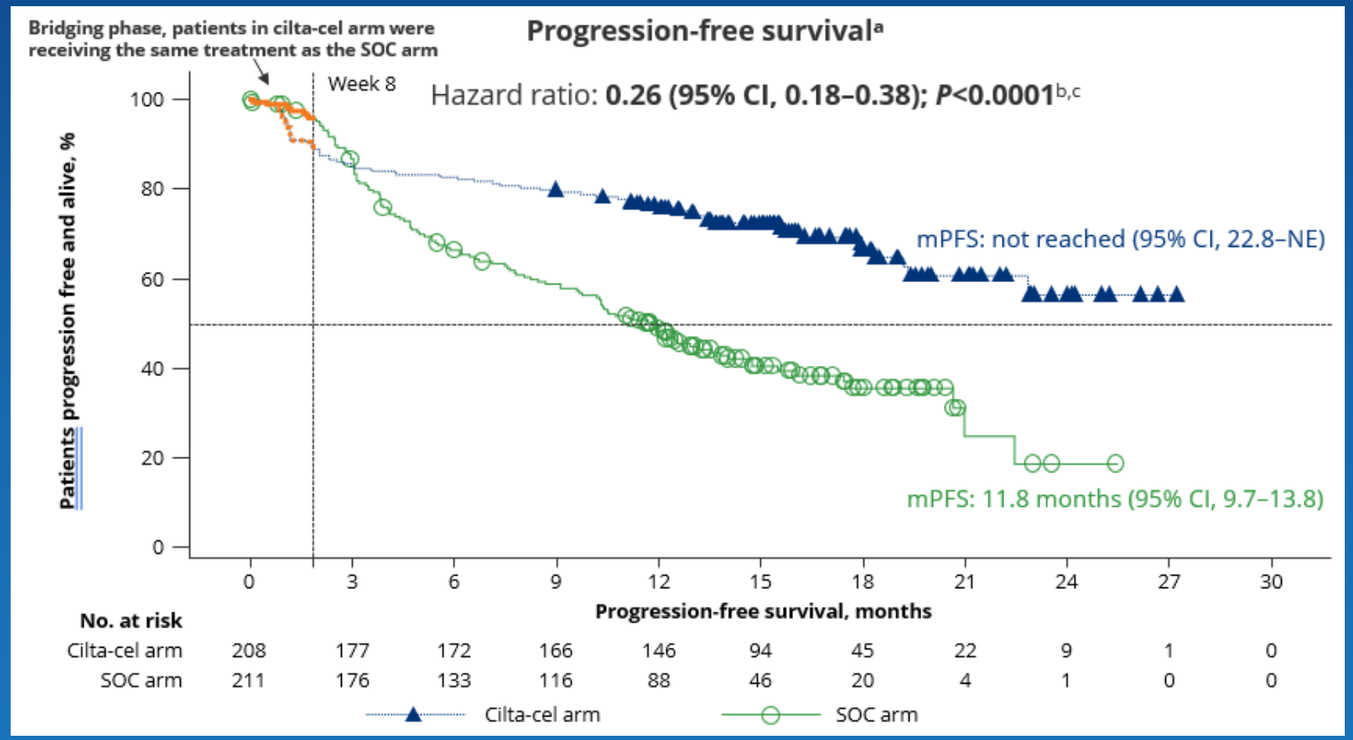
- 12-month PFS rate: 76% vs 49%
- SOC performed as expected

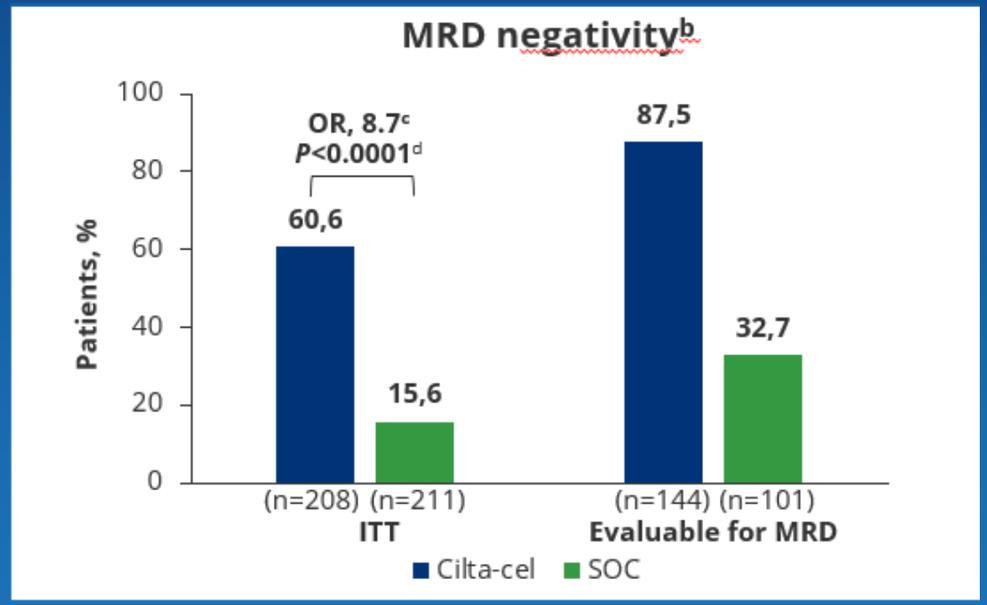
OS: was immature, with 39 deaths in cilta-cel arm vs 47 deaths in SOC arm:

- HR, 0.78; 95% CI, 0.5–1.2, *P*=0.26

MRD: Cilta-cel improved rates of overall MRD negativity[a,b] at 10^{-5} vs SOC

- Cilta-cel provided a significant improvement in depth of response with higher MRD negativity vs SOC



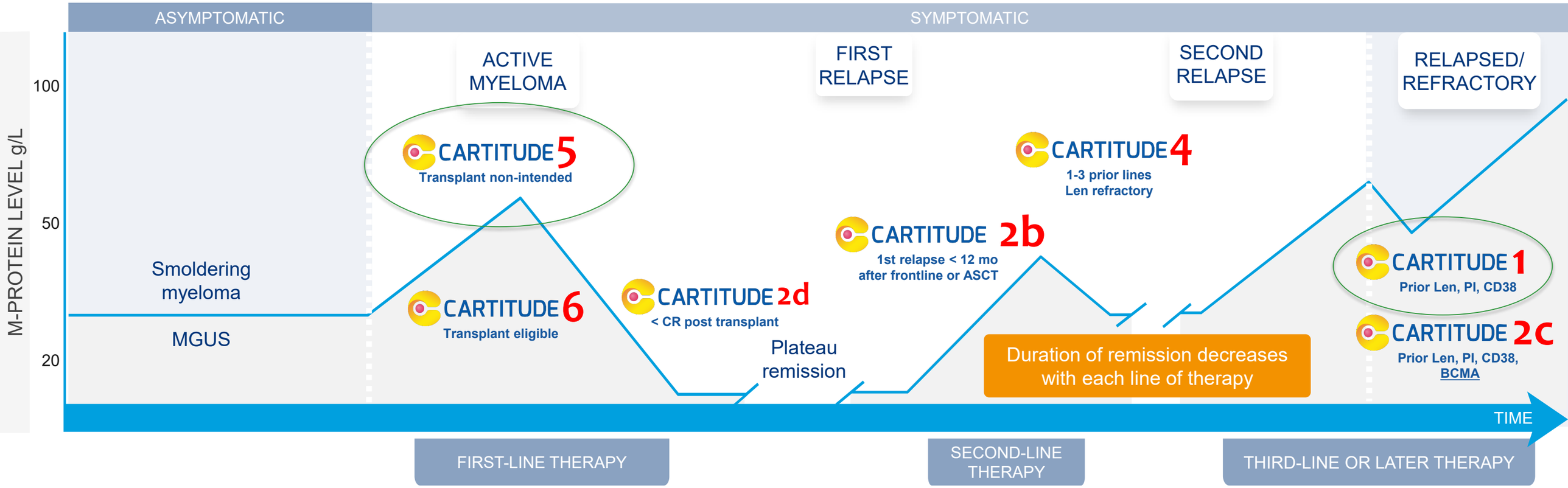


[a]Median follow-up 15.9 months. [b]Constant piecewise weighted log-rank test. [c]Hazard ratio and 95% CI from a Cox proportional hazards model with treatment as the sole explanatory variable, including only progression-free survival events that occurred >8 weeks post randomization.

cilta-cel, ciltacabtagene autoleucel; HR, hazard ratio; ITT, intent-to-treat; mPFS, median progression-free survival; NE, not estimable; SOC, standard of care.

[a]Assessed by next-generation sequencing. [b]Achieved at any time during the study up to data cut-off. [c]Stratified Cochran Mantel-Haenszel test. [d]Fisher's Exact Test
cilta-cel, ciltacabtagene autoleucel; HR, hazard ratio; ITT, intent-to-treat; MRD, minimal residual disease; OS, overall survival; SOC standard of care.

Cilta-cel Clinical Development Program



The unmet need to further improve patient outcomes in myeloma:

- MM remains incurable in most patients, because tumour clones can become resistant to treatment[2,3]
- As MM progresses, each subsequent line of treatment is associated with a shorter progression-free period and decreased rate, depth, and duration of response, as well as worsening of health-related quality of life[1,4-6]

LEGEND BIOTECH

LEGEND-2 (R/R MM)
CARTIFAN-1 (prior PI+IMiD)

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Abbreviations: MGUS, monoclonal gammopathy of undetermined significance; MM, multiple myeloma; RRMM, relapsed or refractory multiple myeloma.

References: 1. Kurtin SE. J Adv Pract Oncol. 2013;4(6 (Suppl 1)):1-14; **2.** Abdi et al. Oncotarget. 2013;4:2186–207; **3.** Dimopoulos et al. Nat Rev Clin Oncol. 2015 Jan;12(1):42-54; **4.** Yong et al. Br J Haematol. 2016;175:252-264; **5**. Hulin et al. Leuk Res.2017;59:75-84 **6.** Despiégel et al. Clin Lymphoma Myeloma Leuk. 2018;19:e13-28;

TECLISTAMAB & TALQUETAMAB
Tecvayli® & *Talvey®*
-Bispecifische Antikörper

Skin cells at 20x magnification

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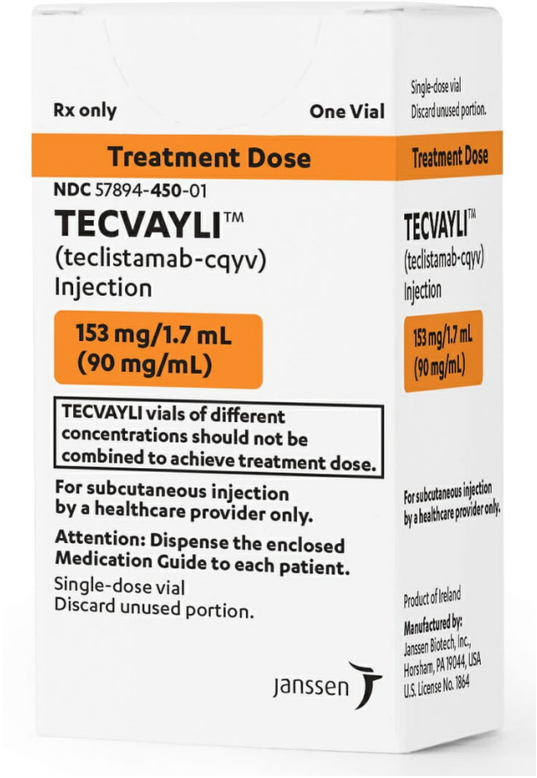
Tecvayli®



Tavley®

s.c. formulation

https://www.drugs.com/image/tecvayli-images.html
https://www.cancertherapyadvisor.com/home/news/conference-coverage/ash-2022/talquetamab-multiple-myeloma-responses-relapsed-refractory/

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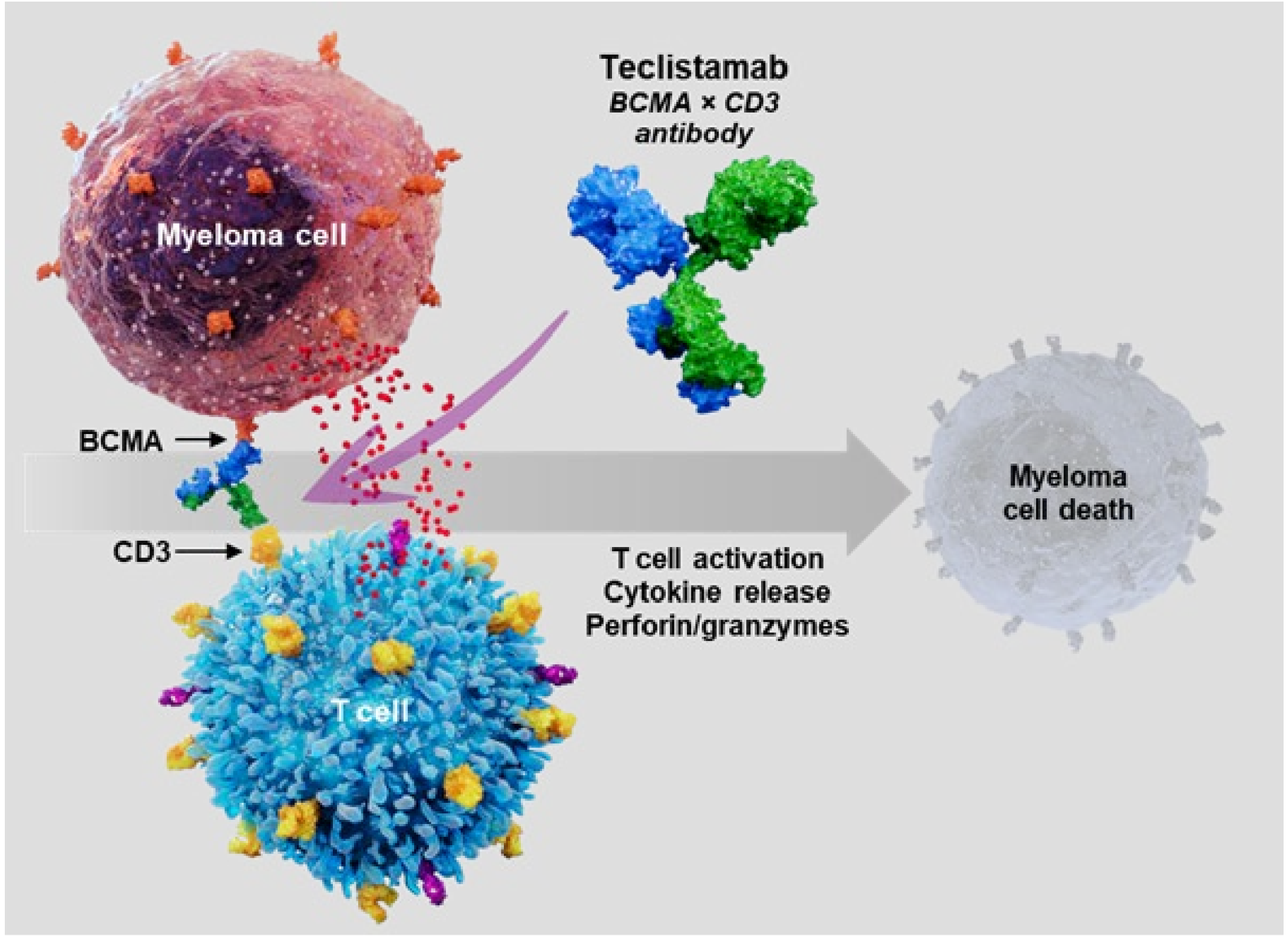
Zulassungstext Tecvayli

TECVAYLI wird angewendet als Monotherapie zur Behandlung erwachsener Patienten mit rezidiviertem und refraktärem multiplen Myelom, die zuvor bereits mindestens drei Therapien erhalten haben, darunter einen immunmodulatorischen Wirkstoff, einen Proteasom-Inhibitor und einen AntiCD38-Antikörper, und die während der letzten Therapie eine Krankheitsprogression gezeigt haben.

Teclistamab: Mode of Action



- Teclistamab (JNJ-64007957) is a humanised IgG-4 **bispecific DuoBody® antibody** that binds to BCMA and CD3
- Preclinical studies have demonstrated that Teclistamab redirects $CD3^+$ T cells to BCMA-expressing myeloma cells to induce cytotoxicity of the targeted cells[1,2]
- Teclistamab potently kills myeloma cell lines and primary myeloma cells from heavily pretreated patients[2]

1. Labrijn AF et al. Proc Natl Acad Sci USA 2013;110:5145.
2. Frerichs KA et al. Clin Cancer Res 2020; 26:2203–21

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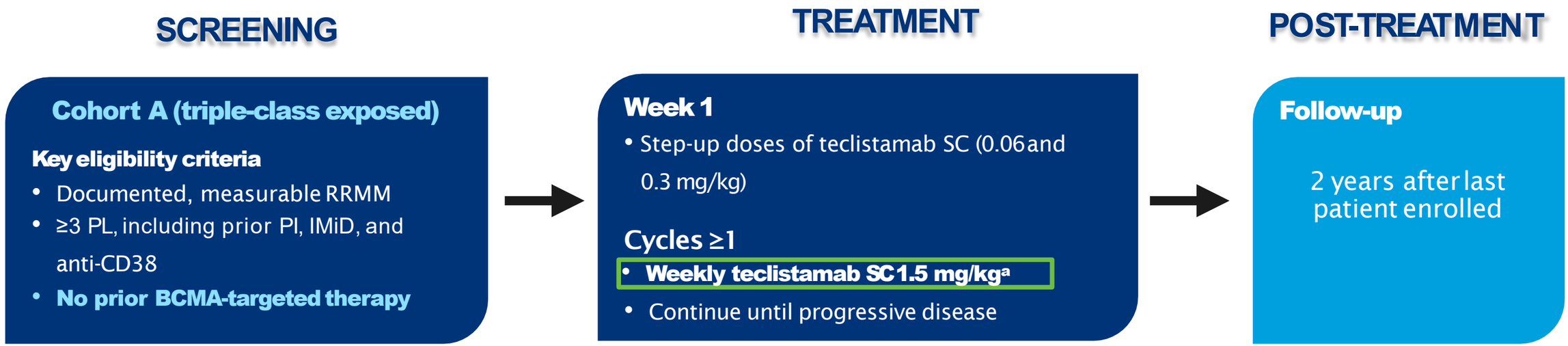
MajesTEC-1: Study Design

- **First-in-human, phase 1/2, open-label, multicohort, multicenter, dose-escalation study evaluating teclistamab in patients with RRMM who previously received ≥3 lines of therapy (triple-class exposed)**



- **Primary endpoint:** ORR
- **Key secondary endpoints:** DOR, ≥VGPR, ≥CR, sCR, TTR, MRD status, PFS, OS, safety, PK, immunogenicity, PROs

[a]Schedule change to biweekly (every other week) dosing was permitted based on response.

BCMA, B-cell maturation antigen; CR, complete response; DOR, duration of response; IMiD, immunomodulatory drug; MRD, minimal residual disease; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PI, proteasome inhibitor; PK, pharmacokinetics; PL, prior line; PRO, patient-reported outcome; RRMM, relapsed/refractory multiple myeloma; sCR, stringent CR; SC, subcutaneous; TTR, time to response; VGPR, very good partial response

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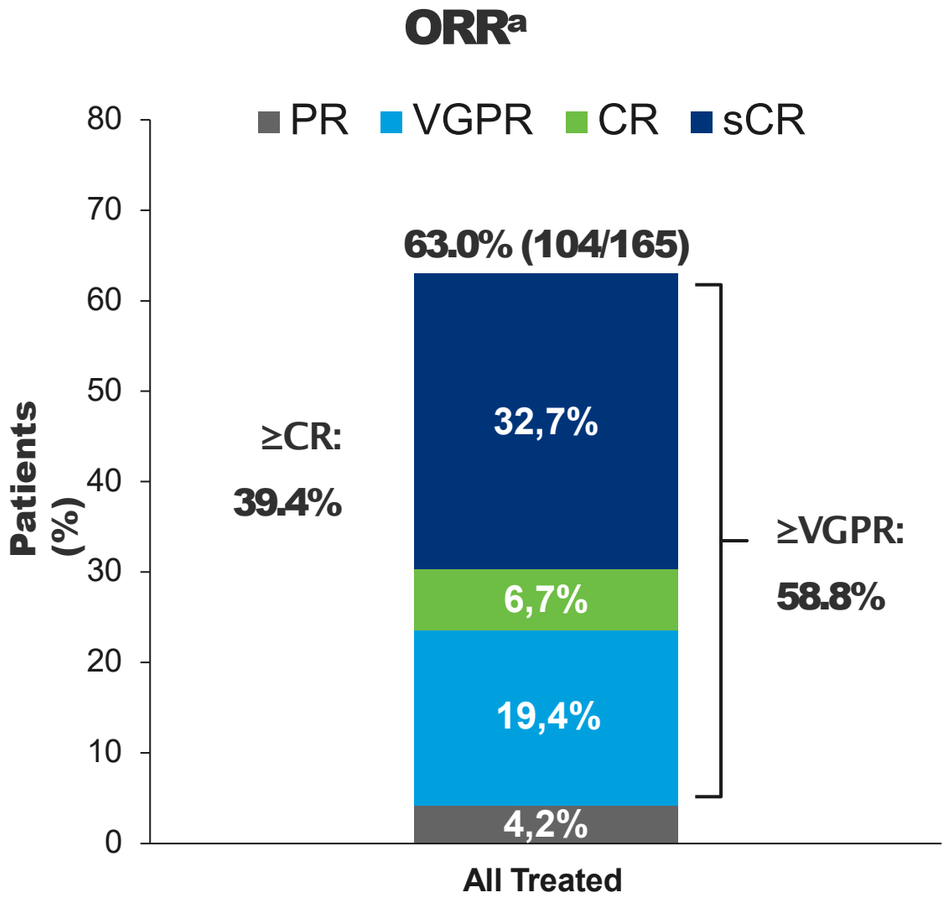
Nooka A., et al Presented at the 2022 American Society of Clinical Oncology (ASCO) Annual Meeting; June 3-7, 2022; Chicago, IL and Virtual.

MajesTEC-1: Overall Response to Teclistamab



ORR of 63.0% (95% CI: 55.2–70.4) represents a substantial benefit for patients with triple-class exposed disease

– Median time to response (n=104)

- First response: 1.2 months (range: 0.2–5.5)
- Best response: 3.8 months (range: 1.1–16.8)

– MRD negativity rate at 10^{-5}[b]

- 26.7% in the all-treated (N=165) patient population
  - 81.5% of MRD-evaluable patients (44 of 54) were MRD negative
- Almost half (46.2%) of patients with ≥CR were MRD negative

Analysis cutoff date: March 16, 2022. [a]PR or better, IRC assessed, per IMWG 2016 criteria. [b]All MRD assessments were done by next-generation sequencing.

CR, complete response; IMWG, International Myeloma Working Group; IRC, independent review committee; MRD, minimal residual disease; ORR, overall response rate; PR, partial response; sCR, stringent complete response; VGPR, very good partial response

Nooka A., et al Presented at the 2022 American Society of Clinical Oncology (ASCO) Annual Meeting; June 3-7, 2022; Chicago, IL and Virtual.

MajesTEC-1: Overall Safety Profile

AEs ≥20%, n (%)	Any Grade	Grade 3/4
Hematologic		
Neutropenia	**117 (70.9)**	**106 (64.2)**
Anemia	**86 (52.1)**	**61 (37.0)**
Thrombocytopenia	**66 (40.0)**	**35 (21.2)**
Lymphopenia	**57 (34.5)**	**54 (32.7)**
Nonhematologic		
CRS	**119 (72.1)**	**1 (0.6)**
Diarrhea	**47 (28.5)**	**6 (3.6)**
Fatigue	**46 (27.9)**	**4 (2.4)**
Nausea	**45 (27.3)**	**1 (0.6)**
Pyrexia	**45 (27.3)**	**1 (0.6)**
Injection site erythema	**43 (26.1)**	**0 (0)**
Headache	**39 (23.6)**	**1 (0.6)**
Arthralgia	**36 (21.8)**	**1 (0.6)**
Constipation	**34 (20.6)**	**0 (0)**
Cough	**33 (20.0)**	**0 (0)**

Teclistamab was well tolerated; discontinuations and dose reductions were infrequent

- 2 patients (1.2%) discontinued due to AEs (grade 3 adenoviral pneumonia; grade 4 PML)
- 1 patient had dose reduction at cycle 21
- The most common AEs were CRS and cytopenias
- Infections occurred in 126 (76.4%) patients (grade 3/4: 44.8%)
- 123 patients (74.5%) had evidence of hypogammaglobulinemia[a]
- There were 19 deaths due to AEs, including 12 COVID-19 deaths
  - 5 deaths due to teclistamab-related AEs:
    - COVID-19 (n=2)
    - Pneumonia (n=1)
    - Hepatic failure (n=1)
    - PML (n=1)

Analysis cutoff date: March 16, 2022. [a]Assessed by AE or lab values (postbaseline IgG level below 500 mg/dL).
AE, adverse event; CRS, cytokine release syndrome; IgG, immunoglobulin G; PML, progressive multifocal leukoencephalopathy

Nooka A., et al Presented at the 2022 American Society of Clinical Oncology (ASCO) Annual Meeting; June 3-7, 2022; Chicago, IL and Virtual.

Teclistamab: Ongoing Studies

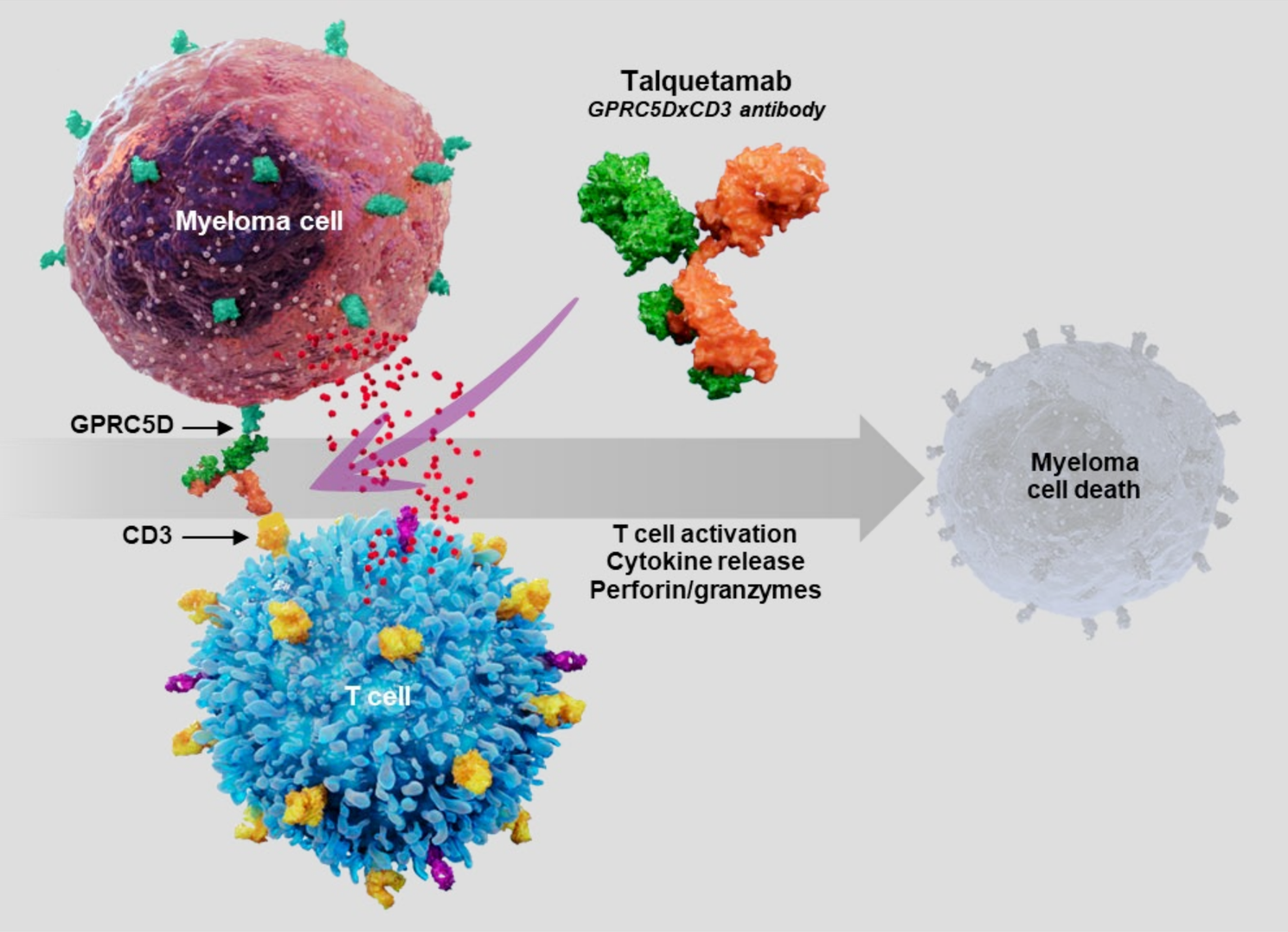
Patients	Study	Phase	Experimental Therapy
R/R MM	MajesTEC-1; MMY1001-P3 (NCT04557098)	II	Teclistamab monotherapy
	MajesTEC-3; MMY3001 (NCT05083169)	III	Teclistamab + daratumumab SC vs. DPd vs DVd
	TRIMM-2; MMY1002 (NCT04108195)	I	Teclistamab + daratumumab SC
	TRIMM-3; MMY1005 (NCT05338775)	Ib	Teclistamab or talquetamab + PD-1 inhibitor
	RedirecTT-1; MMY1003 (NCT04586426)	I	Teclistamab + talquetamab vs. teclistamab + talquetamab + daratumumab SC
NDMM	MajesTEC-4; MMY3003 (NCT05243797)	III	Teclistamab + R vs. R
	MajesTEC-2; MMY1004 (NCT04722146)	I	Teclistamab + daratumumab SC + P vs. teclistamab + daratumumab SC + R

DPd, daratumumab in combination with pomalidomide/dexamethasone; DVd, daratumumab in combination with VELCADE and dexamethasone; MM, multiple myeloma; NDMM, newly diagnosed multiple myeloma; P, pomalidomide; PD-1, programmed cell death protein 1; R, lenalidomide; R/R, relapsed/refractory; SC, subcutaneous.

Zulassungstext Talvey

TALVEY wird angewendet als Monotherapie zur Behandlung erwachsener Patienten mit rezidiviertem und refraktärem multiplem Myelom, die zuvor bereits mindestens 3 Therapien erhalten haben, darunter einen immunmodulatorischen Wirkstoff, einen Proteasom-Inhibitor und einen Anti-CD38-Antikörper, und die während der letzten Therapie eine Krankheitsprogression gezeigt haben.

Talquetamab: Mode of Action



- **Talquetamab is a novel first-in-class, off-the-shelf, T cell-redirecting bispecific antibody** directed against a new antigen target called GPRC5D[2,3]
- **GPRC5D is a novel antigen target in myeloma** that is highly expressed on malignant plasma cells with limited expression in normal human tissues,[4-7] including hematopoietic stem cells[8]

2. Verkleij CPM et al. *Blood Adv* 2021; 5:2196-2215; 3. Pillarisetti K et al. *Blood* 2020; 135:1232-43; 4. Atamaniuk J et al. *Eur J Clin Invest* 2012; 42:953-60; 5. Inoue S et al. *J Invest Dermatol* 2004; 122:565-73.
6. Smith EL et al. *Sci Transl Med* 2019; 11; :eaau7746; 7. Goldsmith R et al. IMW 2021; poster P095. 8. Kodama T et al. *Mol Cancer Ther* 2019; 18:1555-64;

MonumenTAL-1: Study Design

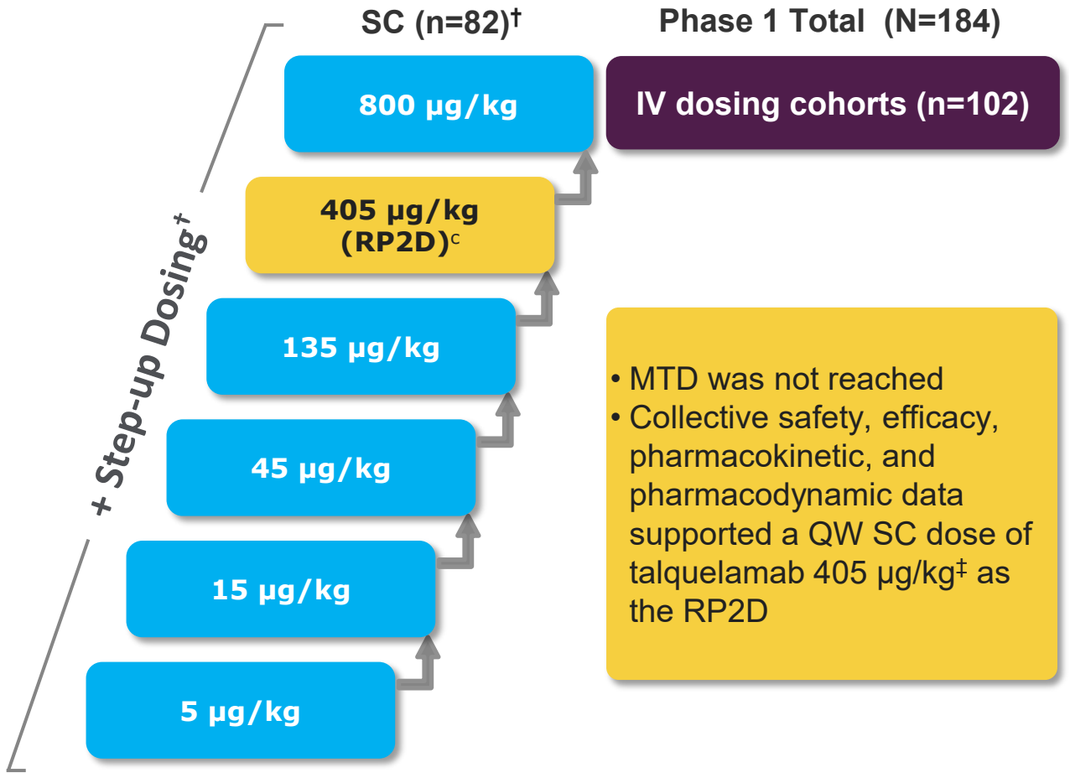
Aim: to present updated results of safety and efficacy of talquetamab at the RP2D, with additional patients and longer follow-up

Eligibility Criteria:
- Adults with measurable MM
- RR or intolerant to established MM therapies
- Hb ≥8 g/dL, platelets ≥50x10^9/L, ANC ≥1.0x10^9/L
- Prior BCMA-targeted therapy allowed

Key objectives :
- Part 1: Identify RP2D
- Part 2: Safety and tolerability at RP2D
- Antitumor activity, PK, PD

Dosing Schedule at RP2D

Step-up doses of 10 µg/kg and 60 µg/kg	405 µg/kg SC (cycle 1 and beyond)		
Week –1	Week 1	Week 2	Week 3
	Tal	Tal	Tal



- MTD was not reached
- Collective safety, efficacy, pharmacokinetic, and pharmacodynamic data supported a QW SC dose of talquelamab 405 µg/kg‡ as the RP2D

- Premedications* were limited to step-up doses and first full dose
  - No steroid requirement after first full dose

*Glucocorticoid, antihistamine, and antipyretic; †1-3 step-up doses given within 1 week before a full dose; ‡Step-up doses of 10 and 60 µg/kg.

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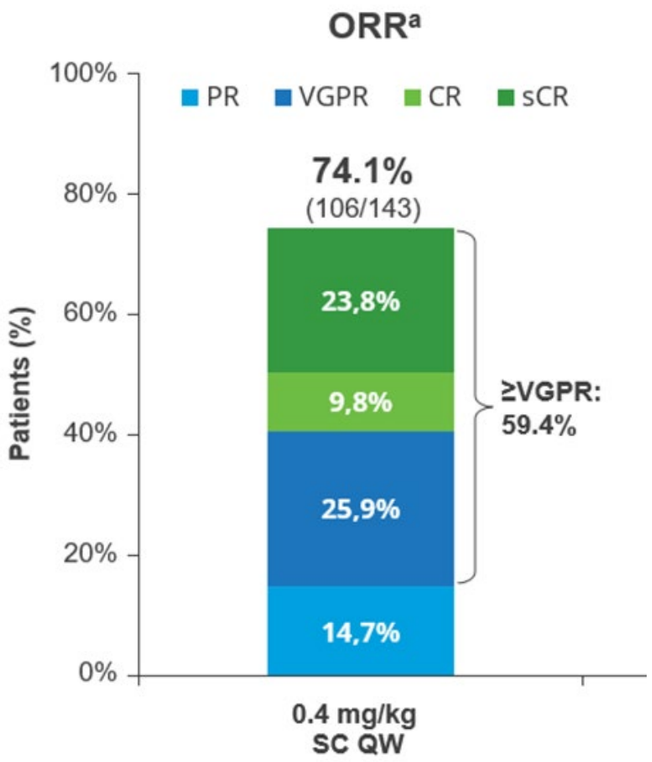
Talquetamab in R/R MM: ORR

Phase I MonumenTAL-1 study (NCT03399799)



ORR >70% in heavily pretreated patients

Median **DOR was 9,3** months (95% CI: 3.0, NE)

Median (range) time to first confirmed response was 0.9 months (0.2–3.8) at 405 µg/kg QW

Minnema M et al. ASCO 2022; poster 8015, Chari A et al. ASH 2022; abstract 157

Talquetamab and Ide-cel have comparable efficacy profiles

Clinical endpoint	Talquetamab[1,2,3] (Janssen) MonumenTAL-1 405ug/kg SC QW	Talquetamab[1,2,3] (Janssen) MonumenTAL-1 800ug/kg SC Q2W	Abecma (ide-cel) BMS KarMMa
OS	Not reported 9-month rate 80.3%	Not reported 9-month rate 82.4%	mOS: 24.8 months
PFS	7.5 months (mDoR)	11.9 months (mPFS)	8.6 months(150-450x10^6) 12.2 months (450x10^6) 5.8 months (300x10^6)
DoR	9.3 months (mDoR)	13.0 months (mDoR)	–
ORR	74% Post-BCMA ADC: 71.4% Post-CAR-T: 68.4% Post-BCMA BsAb: 50.0%	73% Post-BCMA ADC: 75%	73% 50% (150x10^6) 69% (300x10^6) 82% (450 x10^6)
≥CR	33.6%	32.4%	-
≥VGPR	59%	57%	-
Time to response	1.2 months	1.3 months	-
AEs	• Gr 3-4 CRS: 2% • Gr 3-4 Infection: 16% • Gr 3-4 Neurotoxicity: 10.7% (ICANS) • Gr 3-4 Neutropenia: 31%	• Gr 3-4 CRS: 1% • Gr 3-4 Infection: 12% • Gr 3-4 Neurotoxicity: 10.1% (ICANS) • Gr 3-4 Neutropenia: 25%	• Gr 3-4 CRS: 4%/9% • Gr 3-4 Infection: 27% • Gr 3-4 Neurotoxicity: 4% • Gr 3-4 Neutropenia: 91%

Data Cut Reference: September 1, 2022**

**Inclusion criteria in notes

Disclaimer: Indirect comparison

MonumenTAL-1: Non-hematologic safety profile[1]

AEs[a] (≥20% of total SC population), n (%)	405 µg/kg SC QW[b] n=30		800 µg/kg SC Q2W[b] n=44	
	Any grade	Grade 3 / 4	Any grade	Grade 3 / 4
CRS	23 (76.7)	1 (3.3)	35 (79.5)	0
Skin-related AEs[c]	20 (66.7)	0	32 (72.7)	1 (2.3)
Dysgeusia	19 (63.3)	N / A	25 (56.8)	N / A
Nail-related AEs[d]	18 (60.0)	0	15 (34.1)	0
Rash-related AEs[e]	14 (46.7)	1 (3.3)	13 (29.5)	7 (15.9)
Dysphagia	12 (40.0)	0	12 (27.3)	0
Pyrexia	11 (36.7)	0	10 (22.7)	0
Fatigue	10 (33.3)	1 (3.3)	12 (27.3)	0
Dry mouth	9 (30.0)	0	25 (56.8)	0
Weight decreased	9 (30.0)	0	19 (43.2)	1 (2.3)
Nausea	9 (30.0)	0	9 (20.5)	0
Diarrhea	9 (30.0)	0	8 (18.2)	0
ALT increased	6 (20.0)	1 (3.3)	14 (31.8)	3 (6.8)
Decreased appetite	7 (23.3)	1 (3.3)	11 (25.0)	1 (2.3)
Headache	7 (23.3)	0	11 (25.0)	0
AST increased	3 (10.0)	0	14 (31.8)	3 (6.8)

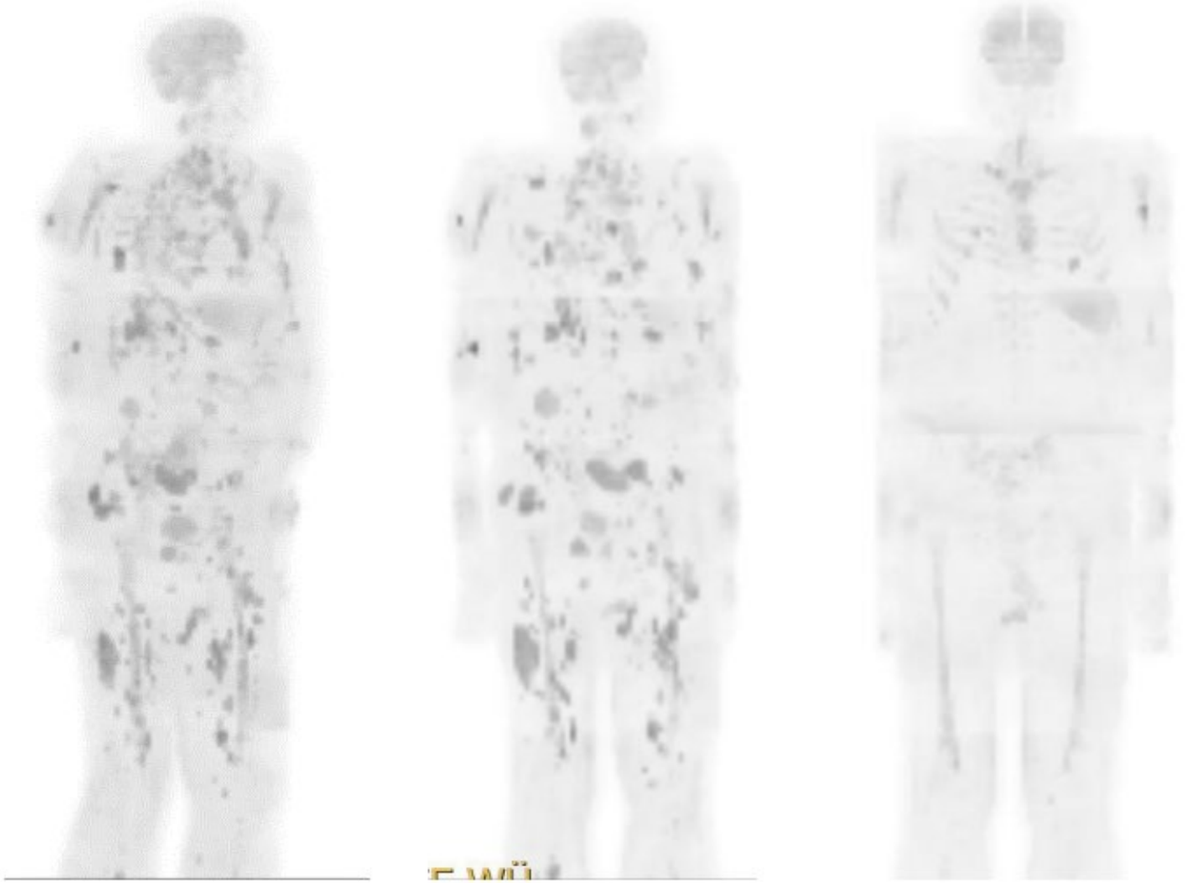
Overall, the most common AEs were CRS, skin-related events, and dysgeusia

- Cytopenias were reversible
- Neutropenias were generally resolved within a week and limited to Cycles 1-2
- Infections occurred in 46.7% of patients at 405 µg/kg QW and 38.6% at 800 µg/kg Q2W (grade 3 / 4: 6.7% / 9.1%)
- Dysgeusia was managed with supportive care, and at times with dose adjustments
- No patients died due to drug-related AEs

1. Minnema M et al. ASCO 2022; poster 8015; 2. Lee DW et al. Blood 2014;124(2):188-95.

Diffusion weighted MRI
(functional imaging)

Pretreatment:
VCD
DRD
DaraPomDex
BCMA Ide-cel 01/21
Dara KTD PACE
Salvage HD Mel 07/21



Jan 2022
Start
Talquetamab

Feb 2022
1week post
Talquetamab-
pseudoprogression

May 2022
After 5 cycles
Talquetamab,
Ifix negative

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TALQUETAMAB

Key facts

1

Wirksamkeit
Bemerkenswert wirkungsvoll: Über 70% Ansprechrate auch bei Patienten mit Hochrisiko-Zytogenetik

2

Vielseitigkeit
Gleichbleibende Wirksamkeit unabhängig von der Exposition gegenüber BCMA-gerichteten Therapien

3

Erhält die Funktion der B-Zellen und des Knochenmarks
B-Zellen bleiben intakt: Geringe Raten von GR >3-Infektionen (12-17%) und Neutropenien (22-31%)

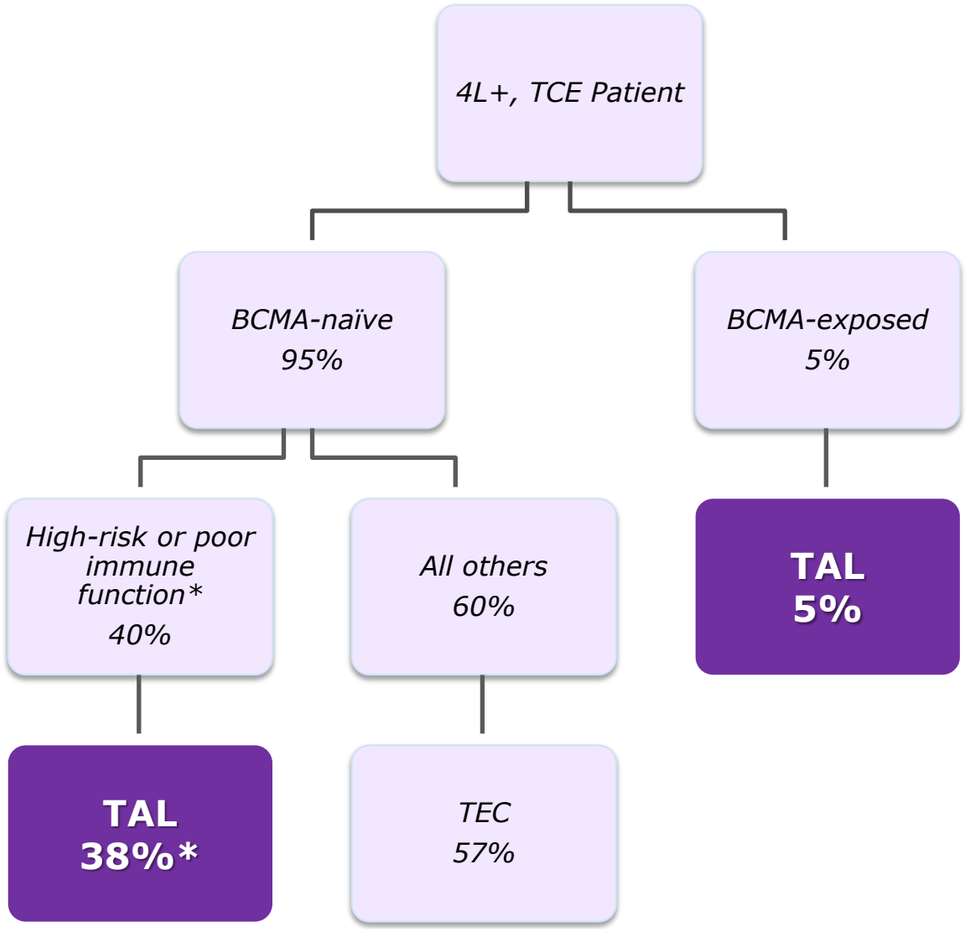
Initial Patient Target

High-Risk

BCMA Exposed and Naïve

Poor Immune Function

Estimated Target Size



*Combined estimate based on high-risk % in Tal-1 (29%) and high risk of infection (~30% based on Dara Gr 3/4 event rates)

BCMA: B-cell maturation antigen **TAL:** Talquetamab **TEC:** Teclistamab

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Geplante Studien mit Teclistamab und Talquetamab in Österreich

Kombinationen

Newly diagnosed MM

- **MAJESTEC-7: TecDR vs. DRd**
- **MAJESTEC-4: TecR vs. R maintenance**

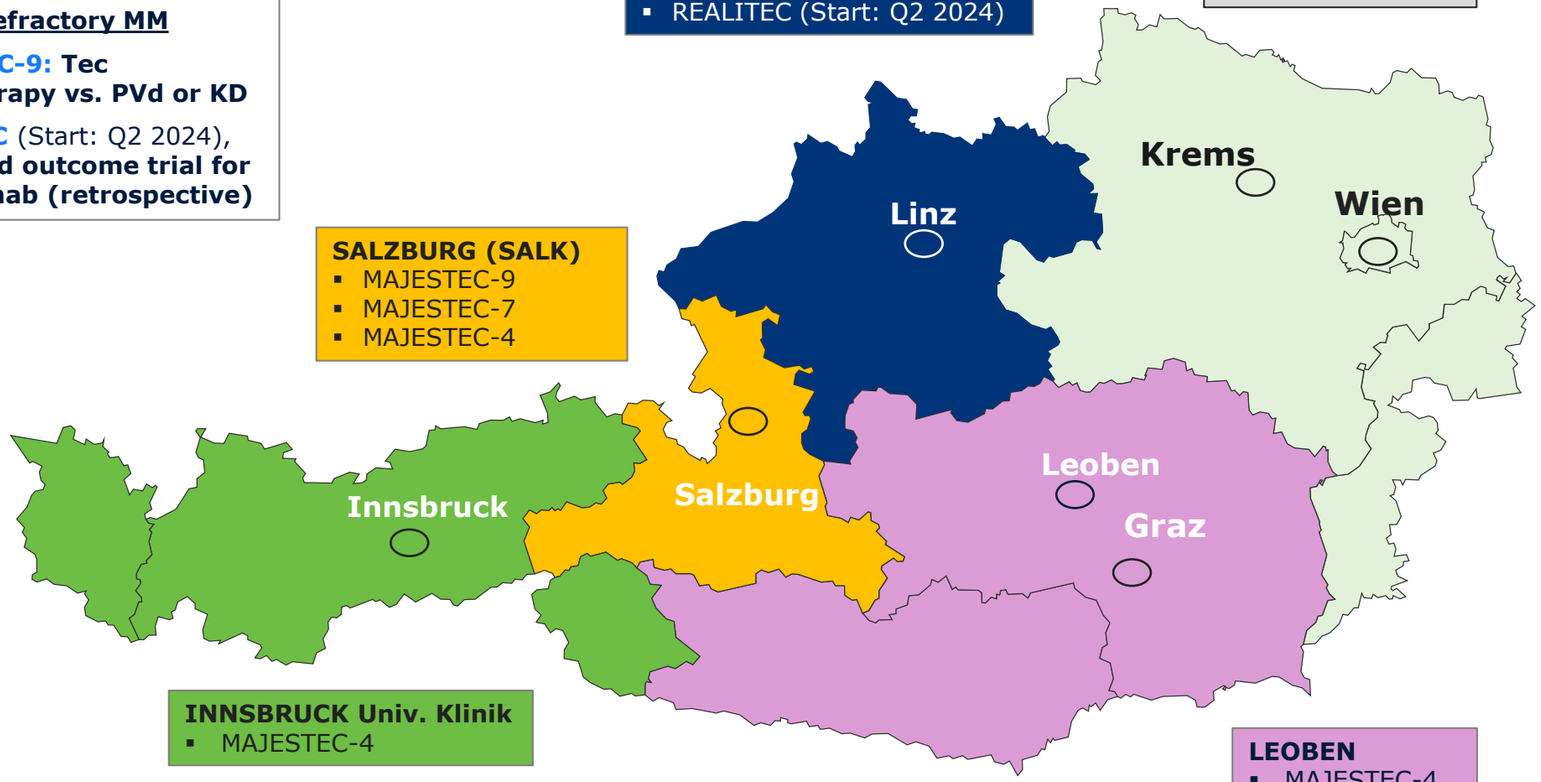
Relapsed/refractory MM

- **MAJESTEC-9: Tec monotherapy vs. PVd or KD**
- **REALITEC** (Start: Q2 2024), **real world outcome trial for Teclistamab (retrospective)**

LINZ Univ. Klinik (KUK)
- MAJESTEC-7
- MAJESTEC-4

LINZ Elisabethinen
- MAJESTEC-7
- MAJESTEC-4
- REALITEC (Start: Q2 2024)

KREMS
- MAJESTEC-4



SALZBURG (SALK)
- MAJESTEC-9
- MAJESTEC-7
- MAJESTEC-4

INNSBRUCK Univ. Klinik
- MAJESTEC-4

LEOBEN
- MAJESTEC-4

WIEN AKH
- MAJESTEC-9
- MAJESTEC-7
- MAJESTEC-4
- REALITEC (Start: Q2 2024)

WIEN Hanusch
- MAJESTEC-7

WIEN Ottakring
- MAJESTEC-4
- REALITEC (Start: Q2 2024)

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Talquetamab: Ongoing Studies

Patients	Study	Phase	Experimental Therapy
R/R MM	MonumenTAL-1 (NCT03399799)	I	Talquetamab monotherapy
	MonumenTAL-1 (NCT04634552)	II	Talquetamab monotherapy
	TRIMM-2; MMY1002 (NCT04108195)	I	Talquetamab + daratumumab SC ± P
	TRIMM-3; MMY1005 (NCT05338775)	Ib	Talquetamab or teclistamab + PD-1 inhibitor
	RedirecTT-1; MMY1003 (NCT04586426)	I	Talquetamab + teclistamab Talquetamab + teclistamab + daratumumab SC
MM	MonumenTAL-2; MMY1004 (NCT05050097)	I	Talquetamab + carfilzomib Talquetamab + daratumumab + K Talquetamab + R Talquetamab + daratumumab + R Talquetamab + P

Please refer to disclaimer slide

D, daratumumab; DPd, daratumumab in combination with pomalidomide/dexamethasone; DVd, daratumumab + bortezomib + dexamethasone; K, carfilzomib; MM, multiple myeloma; NDMM, newly diagnosed multiple myeloma; P, pomalidomide; PD-1, programmed cell death protein 1; R, lenalidomide; R/R, relapsed/refractory; SC, subcutaneous.

Solid Tumors

Pipeline Overview

Skin cells at 20x magnification

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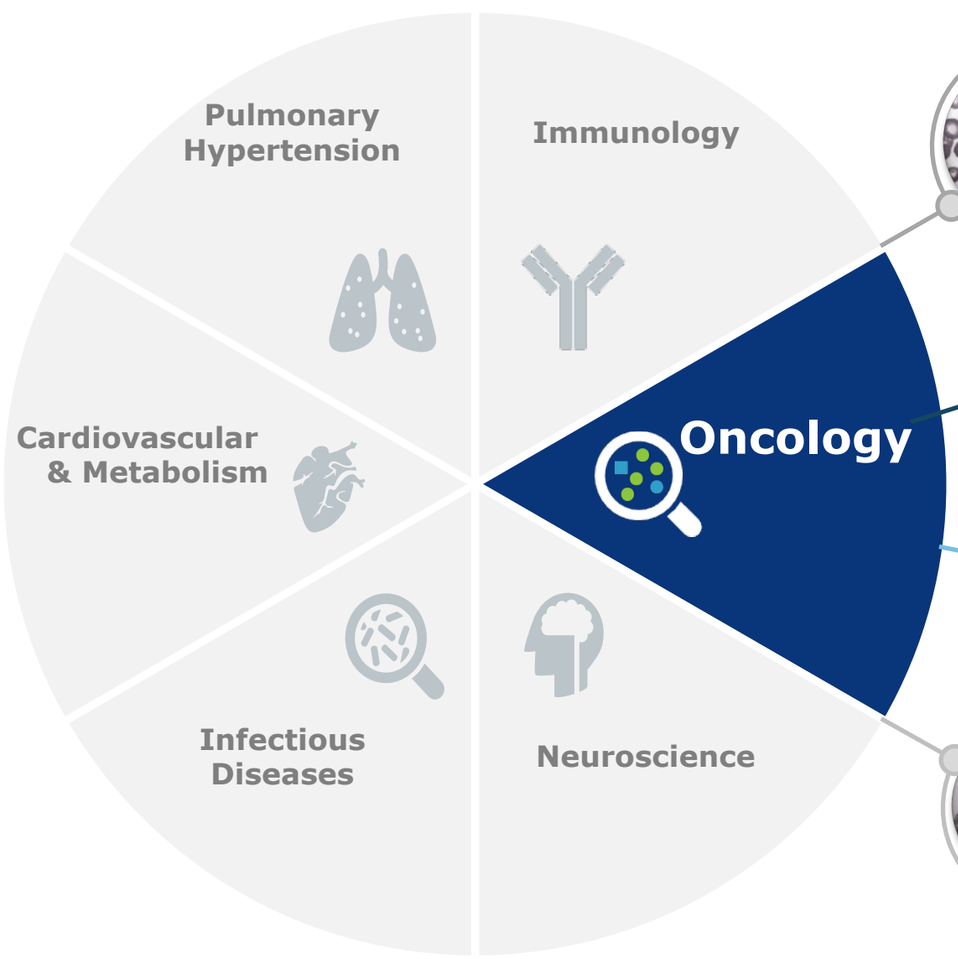
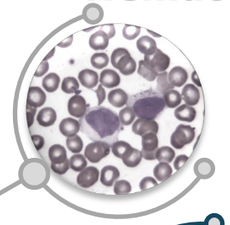
Oncology: Products and Pipeline Substances

Mode of Action

PCa | UC | NSCLC





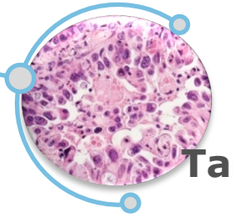
Hematologic Malignancies

Abiraterone Acetate (Zytiga):
Oral CYP17 inhibitor that inhibits androgen biosynthesis in testes, adrenal glands and tumor cells

Apalutamide (Erleada):
Androgen Receptor Inhibitor; blocks androgen binding; prevents nuclear translocation and inhibits transcription

Prostate Cancer

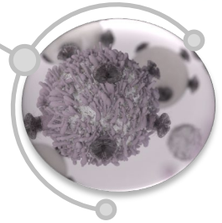
Niraparib + Abiraterone (Akeega):
Oral PARP1/2 inhibitor with synthetic lethality for prostate cancer with DNA repair defects



Solid Tumor Targeted Therapy

Gemcitabine (TARIS) + Cetrelimab
Locally applied CTx + potent and selective PD-1 inhibitor

Erdafitinib (Balversa)
A potent and selective orally available pan-FGFR inhibitor



Immuno-oncology

Amivantamab (Rybrevant): A fully humanized, bispecific IgG1 antibody that targets EGFR and cMET mutations

Lazertinib: Oral, potent, highly mutant-selective, irreversibly binding 3rd-generation EGFR TKI

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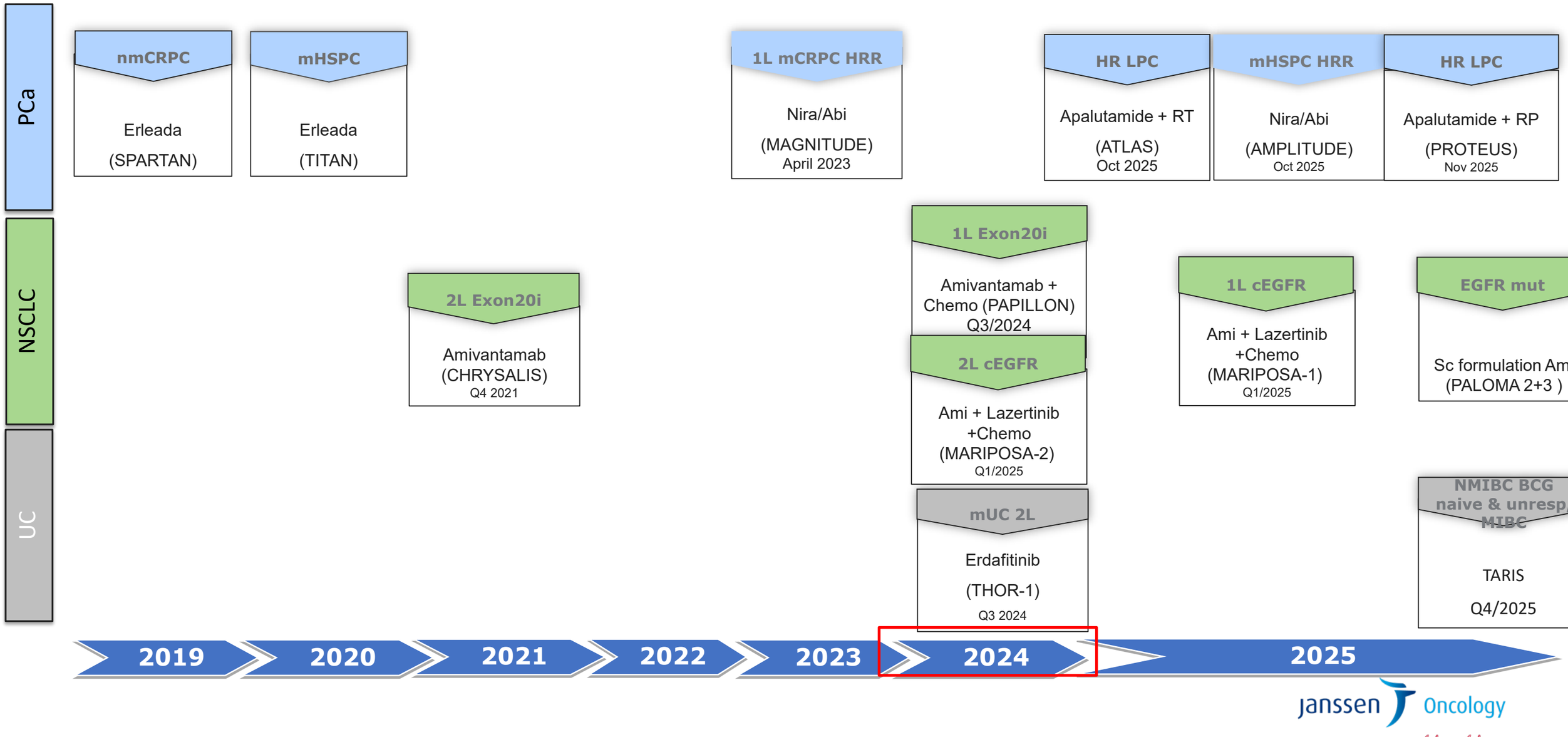
Summary Oncology Portfolio and Pipeline



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AMIVANTAMAB (RYBREVANT®)

Bi-spezfischer Antikörper gegen EGFR und c-MET Mutationen

Skin cells at 20x magnification

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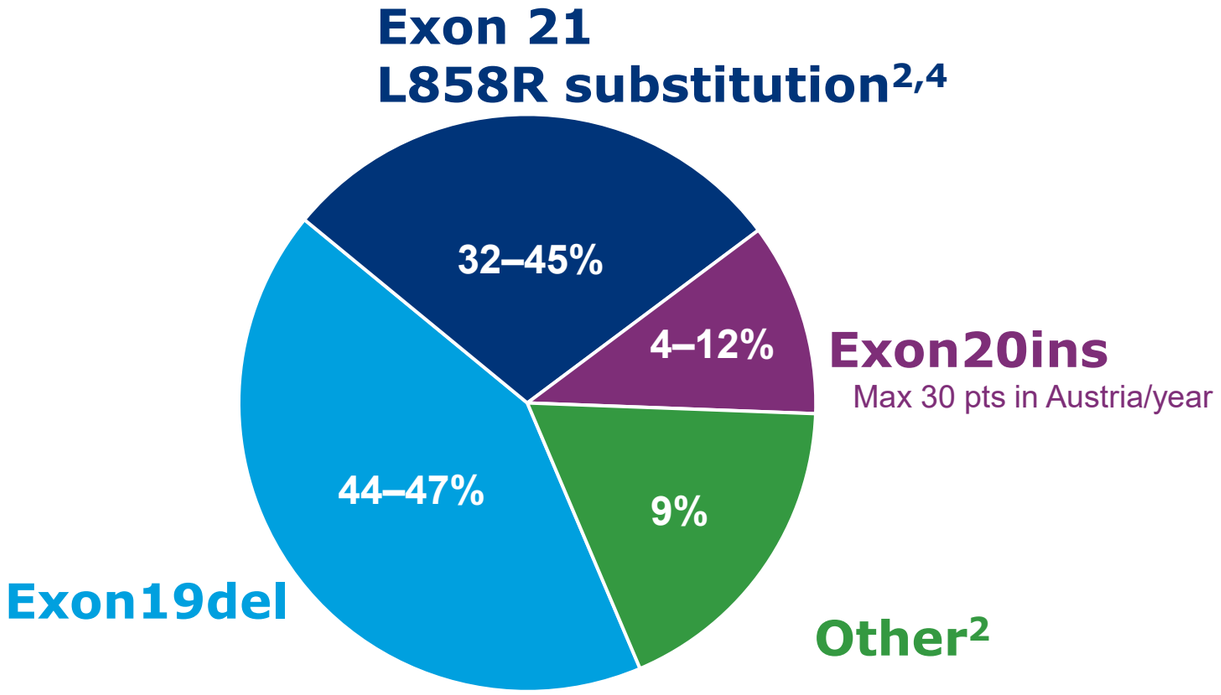
Zulassung Rabrevant®

- Amivantamab als Monotherapie ist indiziert zur Behandlung erwachsener Patienten mit fortgeschrittenem nicht-kleinzelligem Lungenkarzinom und **aktivierenden EGFR Exon-20-Insertionsmutationen** nach Versagen einer platinbasierten Therapie.

Medical Need

In Austria, around 270 patients/year suffer from NSCLC with EGFRmut



Patients with **EGFR exon20ins** have a **poorer prognosis** than those with common EGFR mutations

Graph modified from Reiss et al.[1]

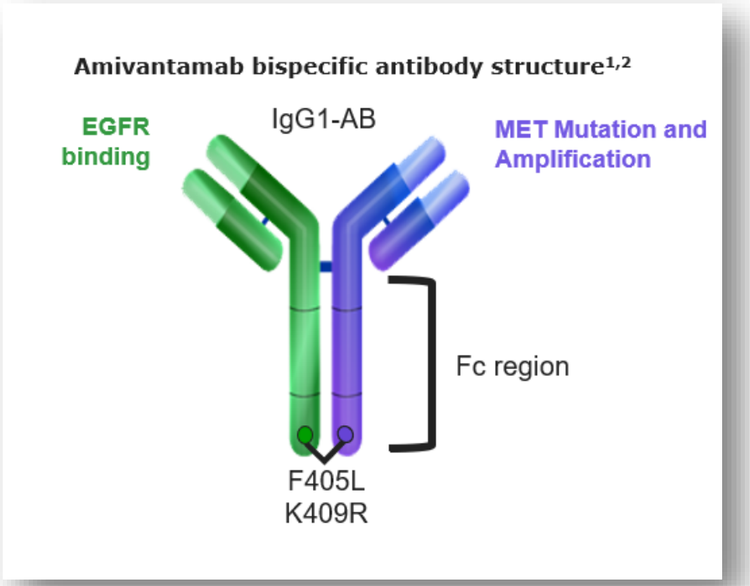
ATP, adenosine triphosphate; ex19del, exon 19 deletion; EGFR, epidermal growth factor receptor; ex20ins, exon 20 insertion mutation; NSCLC, non–small cell lung cancer.

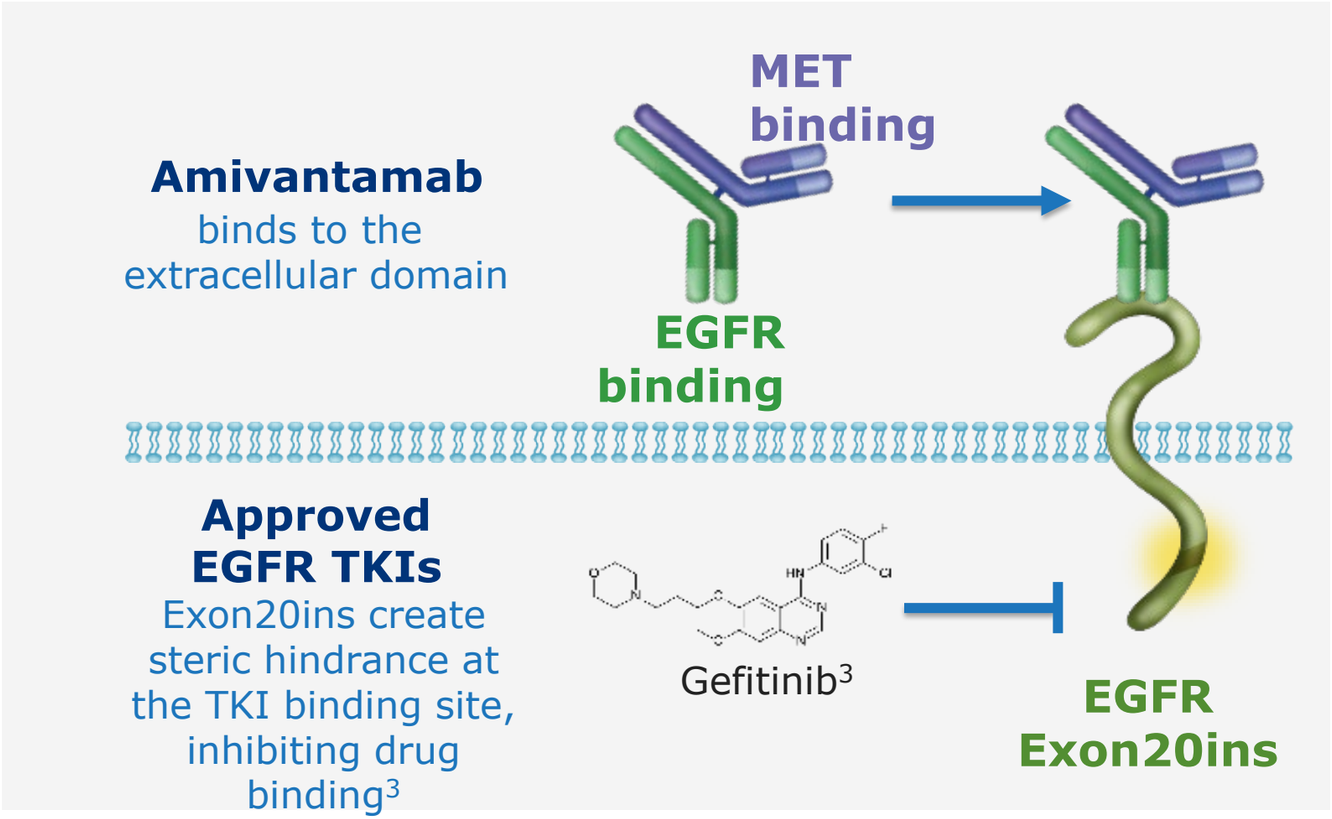
1. Reiss JW, et al. *J Thorac Oncol.* 2018;13(10):1560-1568. 2. Calvayrac O, et al. *Eur Respir J.* 2017;49(4):1601734

Amivantamab

Fully human bispecific antibody that **targets EGFR and MET**,
binding to each receptor's **extracellular domain**, and **bypassing resistance** at the TKI binding site[1,2]

- First bispecific antibody in lung cancer
- Transforms therapy option in Non small cell lung cancer w/EGFRmut
- EGFRexon20ins: No other approved targeted therapies available





NSCLC Non small cell lung cancer; EGFR, epidermal growth factor receptor; EGFRm, EGFR-mutated; ex20ins, exon 20 insertion mutation; IgG, immunoglobulin G; SOC, standard of care; TKI, tyrosine kinase inhibitor. MET mesenchymal–epithelial transition

1. Park K, et al. J Clin Oncol. 2021;39(30):3391–3402; 2. Moores SL, et al. *Cancer Res*. 2016;76(13):3942-3953; 3. Vyse S, Huang PH. Signal Transduct Target Ther. 2019;4:5.

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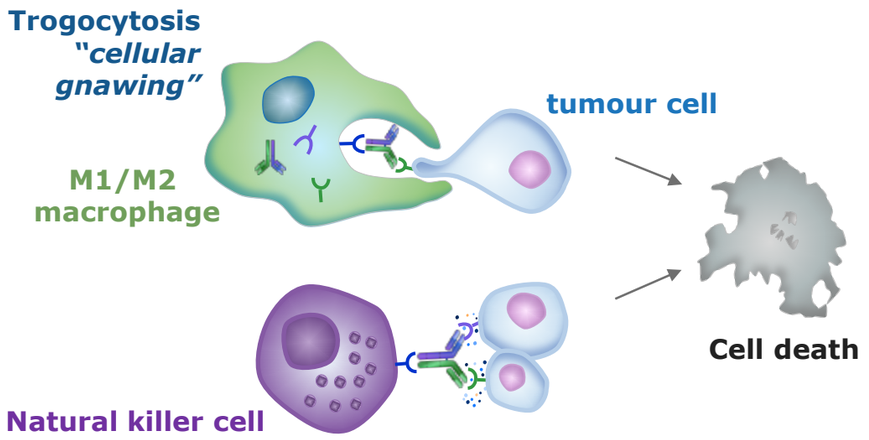
Amivantamab has demonstrated 3 MoAs

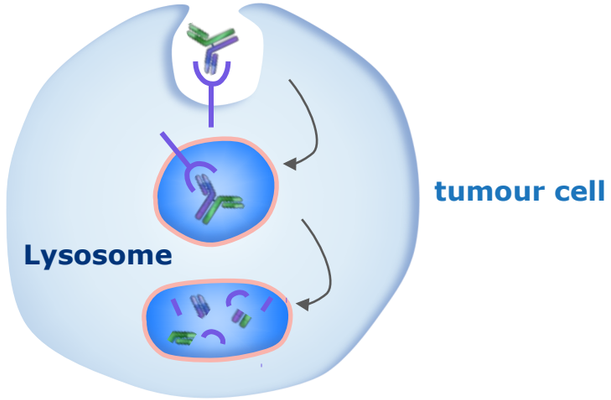
1) Immune activation;
2) Receptor degradation;
3) Inhibition of ligand binding

MoA relevant to EGFR-mutated NSCLC

1. Immune cell–directing activity



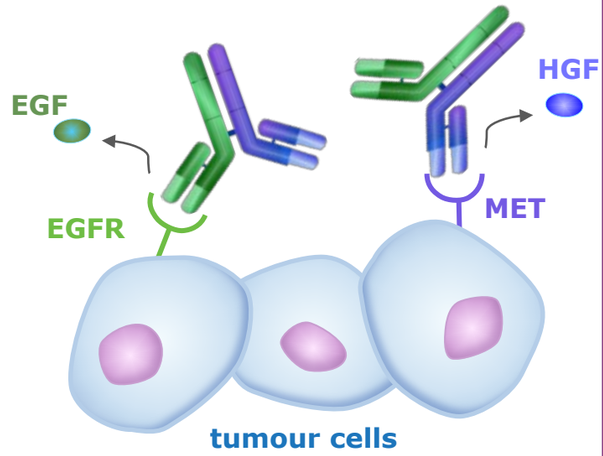
2. Receptor degradation



Trogocytosis also contributes to receptor degradation

MoA relevant to ligand-driven disease

3. Inhibition of ligand binding



EGF, epidermal growth factor (ligand of EGFR), EGFR, epidermal growth factor receptor. HGF, Hepatocyte growth factor (lignad of MET)

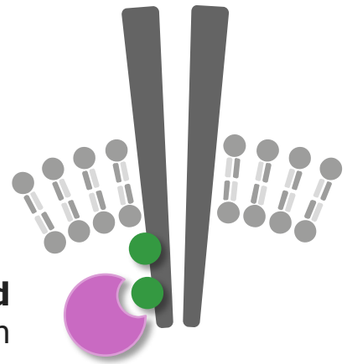
1. Moores SL, et al. *Cancer Res.* 2016;76:3942–3953; 2. Grugan KD, et al. *MAbs*. 2017;9:114–126; 3. Vijayaraghavan S, et al. *Mol Cancer Ther.* 2020;19:2044–2056; 4. Park K, et al. J Clin Oncol. 2021;39(30):3391–3402.

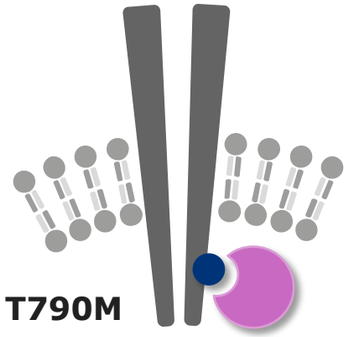
Lazertinib: Third-generation, irreversible, mutation-selective EGFR TKI

1 Inhibits both EGFR sensitising and resistance mutations (T790M)[1,2]

Potently inhibits tumour growth across a range of EGFR models, including those with activating and resistance mutations[1]

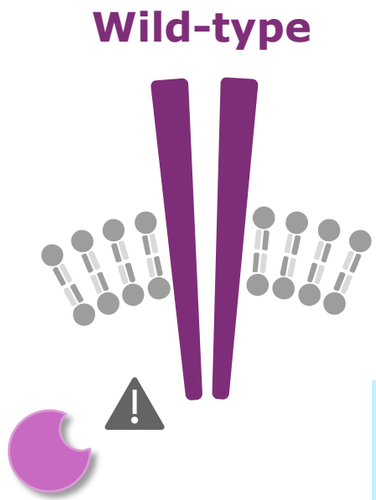
Exon 19 deletion **and** L858R point mutation





T790M is the most common mechanism of resistance to first- or second-generation EGFR TKIs[3]

2 Low activity against wild-type EGFR[1,2]



Binds with low affinity for wild-type EGFR[1]

Penetrates the blood-brain barrier, enabling potent intracranial anti-tumour effects[1]

EGFR, epidermal growth factor receptor; TKI, tyrosine kinase inhibitor.

1. Yun J, et al. *Clin Cancer Res.* 2019;25:2575–2587; 2. Ahn M-J, et al. Poster presentation at ASCO 2019 Congress, Chicago, USA; abstract 9037; 3. Yu HA, et al. *Clin Cancer Res*. 2013;19(8):2240–2247.

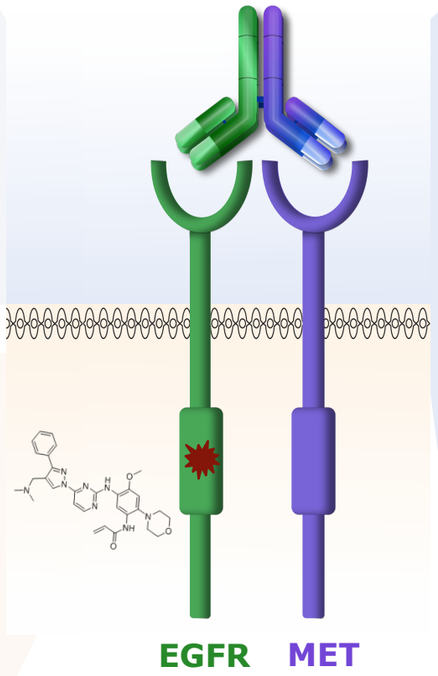
Rationale combining Amivantamab and Lazertinib

Amivantamab

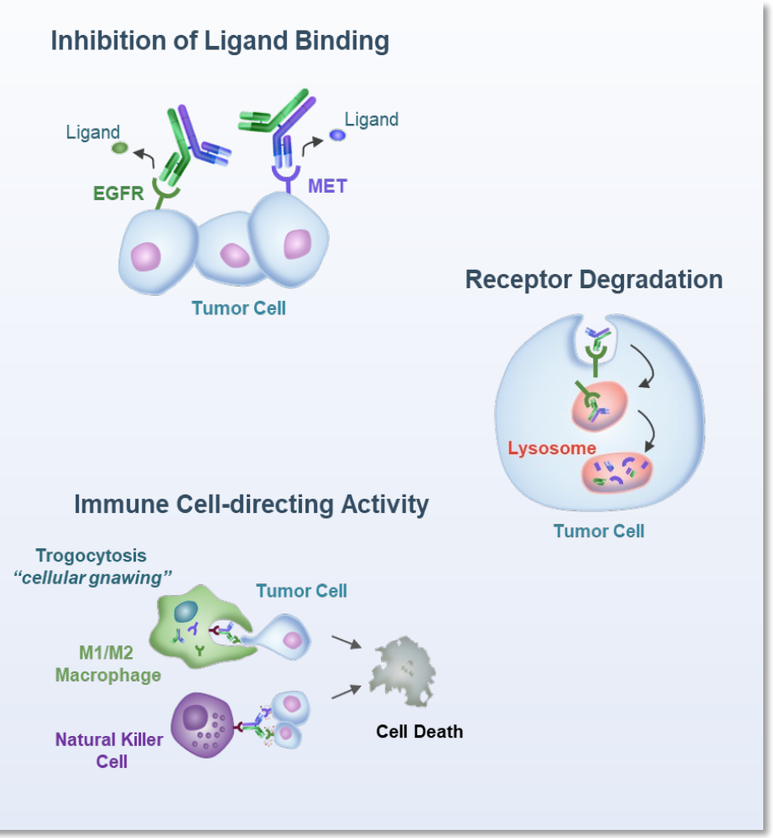
- Fully human bispecific antibody that targets EGFR and MET
- Fc portion has immune cell-directing activity[1]
- Demonstrated clinical activity across diverse EGFRm NSCLC[2-4]
- Granted Breakthrough Therapy Designation for EGFRm Exon20ins NSCLC post-chemotherapy in US and China

Lazertinib

- Potent 3rd-gen TKI with efficacy in activating EGFR mutations, T790M, and CNS disease[5-6]
- Low rates of EGFR-related toxicity such as rash and diarrhea[5]
- Low cardiovascular safety risk[7]
- Safety profile that supports combination with other anti-EGFR molecules



Amivantamab MOA

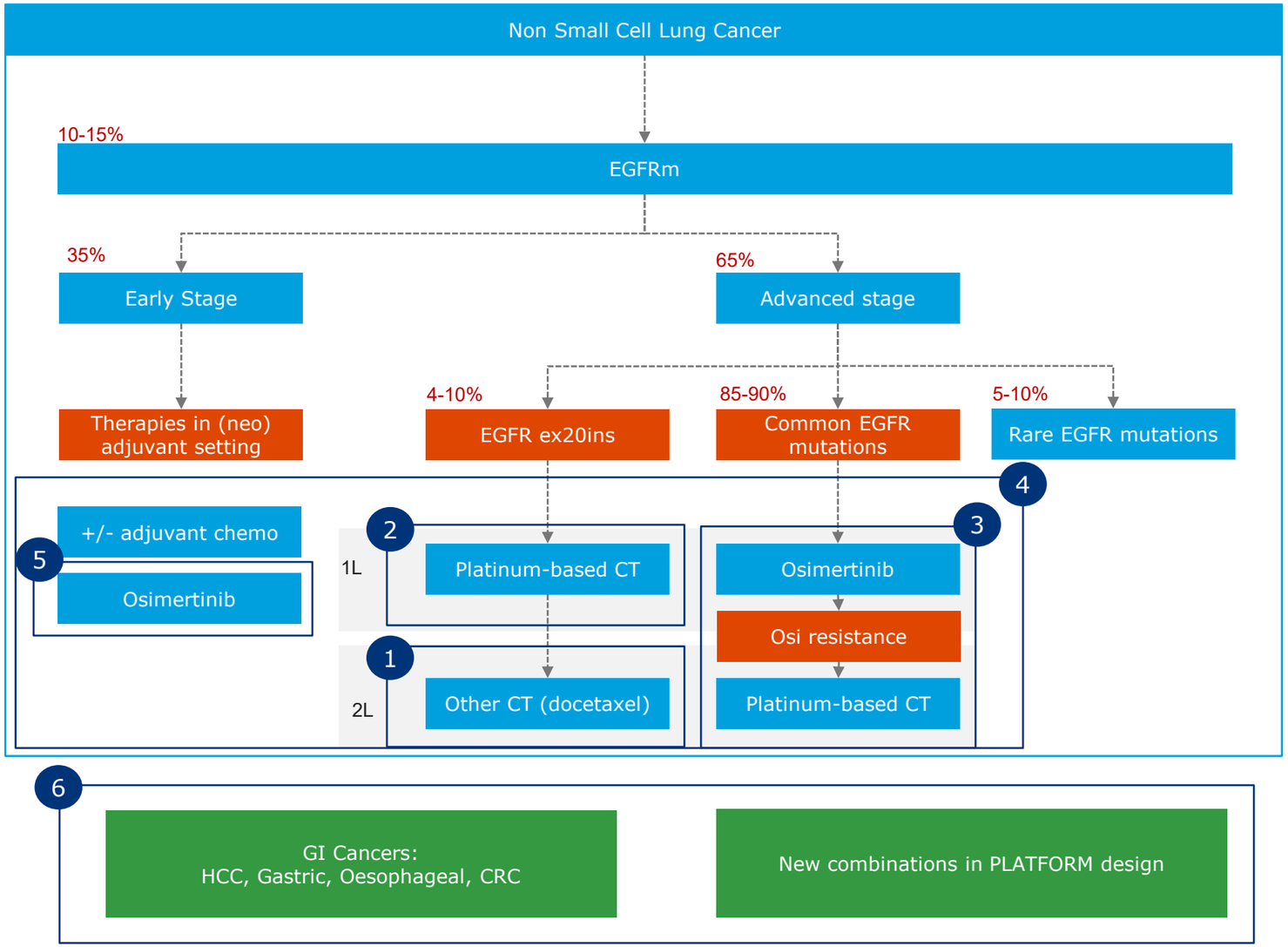


BTD, Breakthrough Therapy Designation; CNS, central nervous system; EGFRm, epidermal growth factor receptor mutant; gen, generation; MOA, mechanism of action; NSCLC, non-small cell lung cancer; TKI, tyrosine kinase inhibitor.

1. Vijayaraghavan *Mol Cancer Ther*. 19:2044; 2. Haura *JCO*. 37:9009 (oral); 3. Park *JCO* 38:9512 (poster); 4. Sabari *JTO* 16:S108 (oral); 5. Ahn *Lancet Oncol* 20:P1681; 6. Kim *JCO* 38:9571 (poster); 7. Haddish-Berhane *JTO* 16:S677 (poster).

Bauml JM, et al. Oral presentation at ASCO 2021; abstract 9006.

Amivantamab clinical development plan



Anticipated regulatory timelines

2022

1 **CHRYSALIS (cohort D)**
Amivantamab monotherapy in 2L+ EGFR exon20ins (post platinum)

2023

2024

2 **PAPILLON**
Amivantamab + doublet chemo in FL EGFR exon20ins

MARIPOSA-2
Amivantamab + lazertinib + doublet chemo in 2/3L cEGFR (post-osi)

2025

3 **MARIPOSA**
Amivantamab + lazertinib in FL cEGFR

2026 +

4 **PALOMA-3 + PALOMA-2**
Subcutaneous formulation for amivantamab

5 **ADONIS**
Amivantamab + lazertinib in adjuvant NSCLC cEGFR MRD+

6 **Beyond EGFR+ NSCLC**
GI cancers and in new combinations

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Amivantamab/Lazertinib Clinical Development Program

NSCLC

CHRYSALIS
First-in-Human Phase 1
Amivantamab +/- Lazertinib

CHRYSALIS-2
Phase 1b
Amivantamab+Lazertinib
Combo

MARIPOSA
Phase 3
Amivantamab+Lazertinib
Combo

PAPILLON
Phase 3
Amivantamab+
Carbo/Pemetrexed

MARIPOSA-2
Phase 3
Ami+Lazertinib+
Carbo/Pemetrexed

PLATFORM
Phase 1/2
Amivantamab
Combinations

Other Formulation

PALOMA
Phase 1
Amivantamab

Paloma-3
Sub-Q
Phase 3
Amivantamab

Paloma-2
Sub-Q
Phase 2
Amivantamab

Other Tumor Types

Gastric/Esophageal Cancer (Japan)
Colorectal Cancer (Global)
Hepatocellular Carcinoma (China)
Head & Neck (Global)

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PAPILLON (NCT04538664)

A **Phase III randomized** study of **amivantamab and carboplatin-pemetrexed** versus carboplatin-pemetrexed in participants with *EGFR* exon20ins mutated locally advanced or metastatic NSCLC

N=308

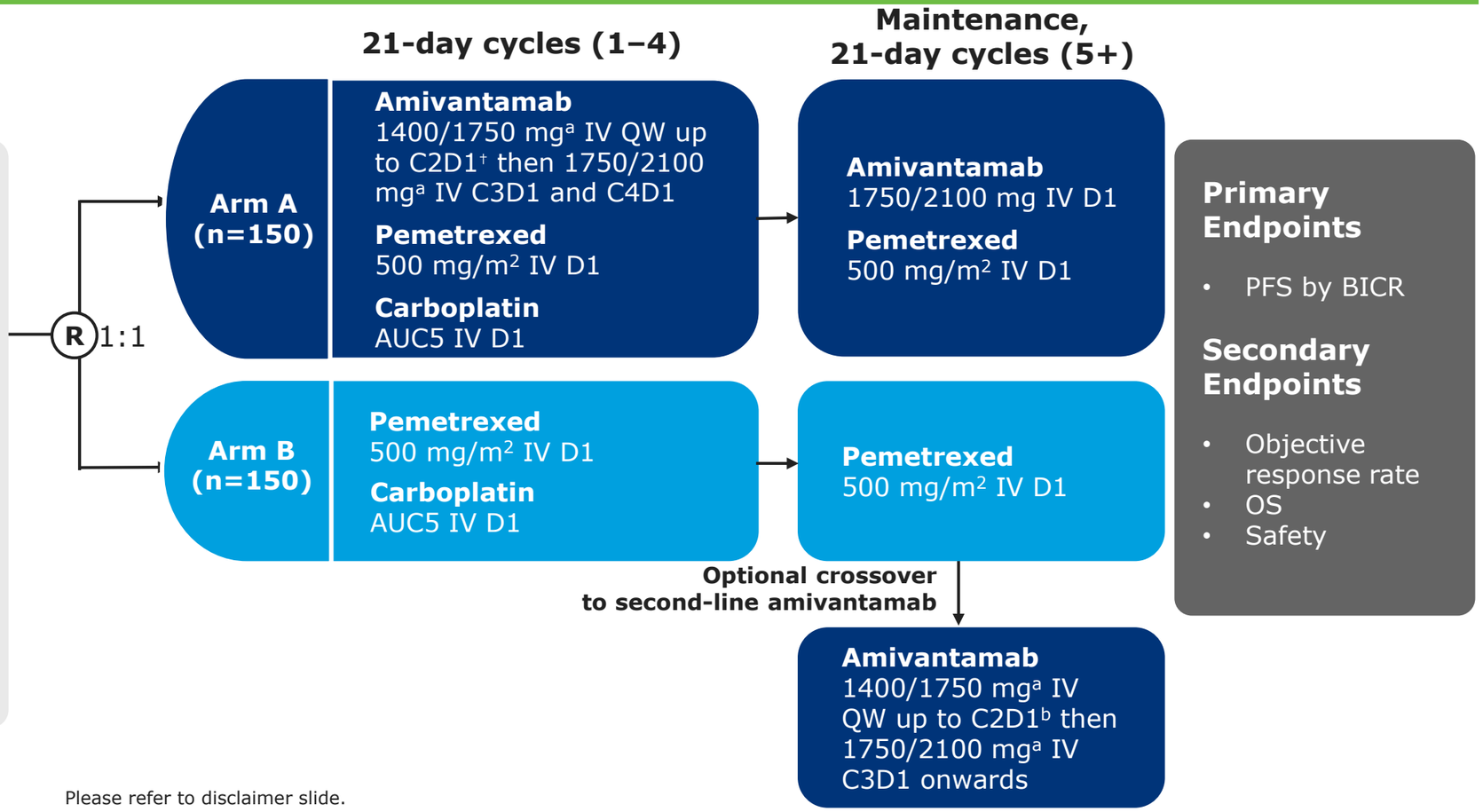
Key Eligibility Criteria:

- Untreated locally advanced or metastatic NSCLC
- Documented *EGFR* exon20ins activating mutation

Stratification:

- Brain metastases (yes/no)
- ECOG status (0/1)
- Prior EGFR TKI treatment (yes/no)

200 sites in 25 countries



Please refer to disclaimer slide.

[a]Dose by weight (<80 kg/≥80 kg); [b]C1: D1/2 (split dose), 8, 15; C2: D1.

AUC, area under the curve; BICR, blinded independent central review; C, Cycle; D, Day; ECOG, Eastern Cooperative Oncology Group; *EGFR*, epidermal growth factor receptor; IV, intravenous; NSCLC, non-small-cell lung cancer; OS, overall survival; PFS, progression-free survival; QW, once weekly; TKI, tyrosine kinase inhibitor.

Agrawal T, et al. WCLC 2020: abstract 3380 (poster presentation).

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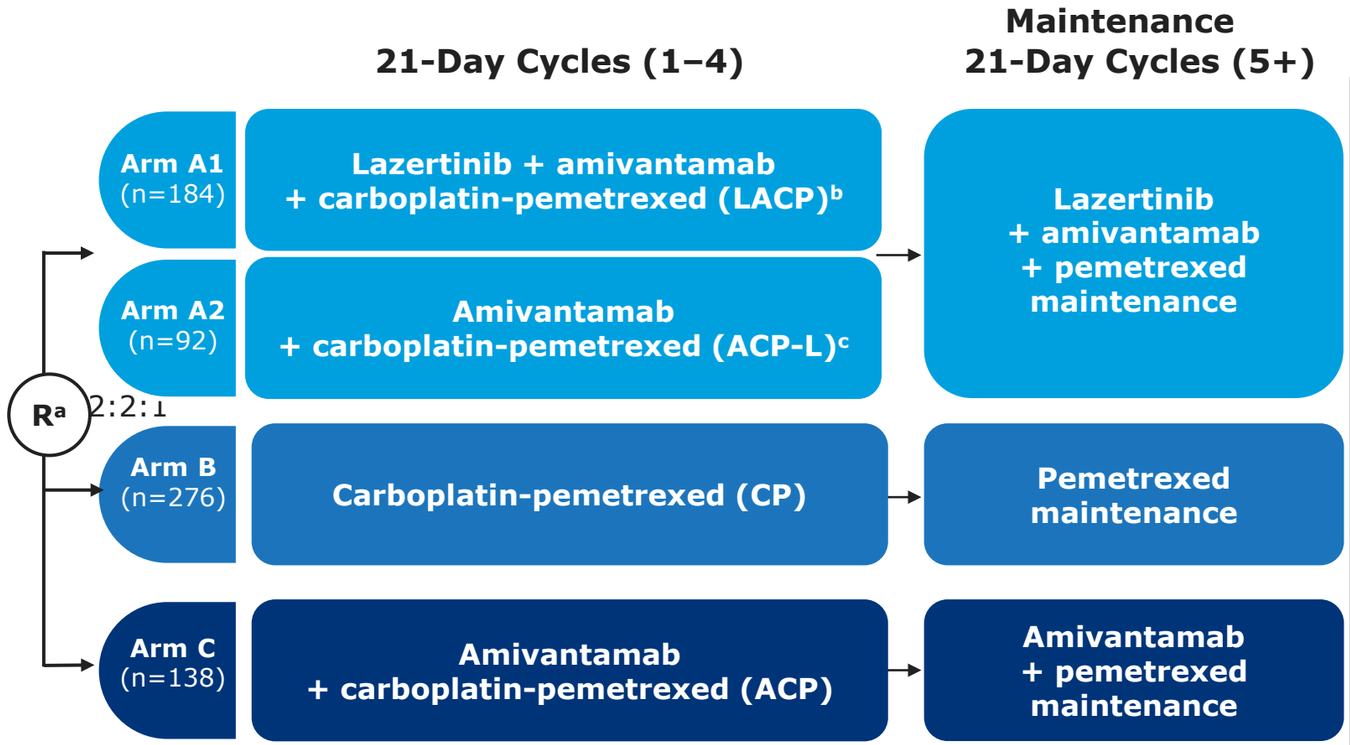
MARIPOSA-2 (NCT04988295)

A **randomized Phase III** study of **amivantamab** and **lazertinib** with **platinum-based chemotherapy** versus **platinum-based chemotherapy** in participants with *EGFR*m+ locally advanced or metastatic NSCLC after osimertinib

N=~690

Key Eligibility Criteria:

- Locally advanced or metastatic NSCLC
- ≥1 measurable lesion (RECIST v1.1)
- Progressed on or after osimertinib monotherapy as the most recent line of treatment



Primary Endpoint

- PFS by BICR

Secondary Endpoints

- Objective response rate
- OS
- DoR
- Time to subsequent therapy
- PFS2
- Time to symptomatic progression
- Intracranial PFS
- Safety

Please refer to disclaimer slide.

[a]Stratification factors: osimertinib line of therapy (1L vs. 2L), history of brain metastases (yes vs. no), Asian race (yes vs. no); [b]LACP dosing strategy from study start until 6 November 2022; [c]ACP-L dosing strategy from 7 November 2022 until last patient in. Lazertinib in ACP-L will start on Cycle 5 Day 1 or sooner if carboplatin is discontinued before Cycle 4.

1L, first-line; 2L, second-line; BICR, blinded independent central review; DoR, duration of response; *EGFR*m+, epidermal growth factor receptor-mutated; NSCLC, non-small cell lung cancer; OS, overall survival; PFS, progression-free survival; PFS2, progression-free survival after subsequent therapy; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1.

MARIPOSA (NCT04487080)

A **Phase III randomized** study of **amivantamab** and **lazertinib** versus **osimertinib** versus **lazertinib** as 1L treatment in participants with ***EGFR*m+** locally advanced or metastatic **NSCLC**

N=1074

Key Eligibility Criteria:

- Locally advanced or metastatic *EGFR*m+ NSCLC
- L858R or Exon19del
- No prior chemotherapy for advanced disease
- No history of ILD/pneumonitis
- No symptomatic brain metastases
- ≥1 measurable lesion per RECIST v1.1

R

Arm A Open-label: **Amivantamab** 1050 mg (body weight <80 kg) or 1400 mg (body weight ≥80 kg) IV[a] + **lazertinib** 240 mg PO QD

Arm B Blinded: **Osimertinib** 80 mg PO QD + **placebo**[b]

Arm C Blinded: **Lazertinib** 240 mg PO QD + **placebo**[c]

Primary Endpoint

- PFS by BICR

Secondary Endpoints

- ORR
- OS
- DoR
- TTSP
- PFS2
- Intracranial PFS
- Safety
- Change from baseline in NSCLC-SAQ and EORTC-QLQ-C30
- Serum concentration of amivantamab
- Plasma concentration of lazertinib
- ADAs

Please refer to disclaimer slide.
[a]Once weekly in Cycle 1 (split dose on Days 1–2), and then every 2 weeks in subsequent cycles. [b]Placebo lazertinib. [c]Placebo osimertinib.
1L, first-line; ADA, anti-drug antibody; BICR, blinded independent central review; DoR, duration of response; *EGFR*m+, epidermal growth factor receptor-mutated; EORTC QLQ-C30, The European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; ILD, interstitial lung disease; IV, intravenous; NSCLC, non-small cell lung cancer; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PFS2, progression-free survival after subsequent therapy; PO, orally; QD, once daily; QW, once-weekly; RECIST, response evaluation criteria in solid tumors; SAQ, Symptom Assessment Questionnaire; TTSP, time to symptomatic progression.

Verabreichungs- und Dosierschema Amivantamab:
i.v. in den ersten 4 Wochen wöchentlich, danach alle zwei Wochen

Infusion Rates for Amivantamab Administration

3-4 Stunde Infusionsdauer

1050-mg Dose (<80 kg)			
Week	**Dose (per 250-mL bag)**	**Initial infusion rate**	**Subsequent infusion rate†**
Week 1 (split dose infusion)			
Week 1 day 1	350 mg	50 mL/hr	75 mL/hr
Week 1 day 2	700 mg	50 mL/hr	75 mL/hr
Week 2	1050 mg	85 mL/hr	
Subsequent weeks*	1050 mg	125 mL/hr	

3-4 Stunde Infusionsdauer

1400-mg Dose (≥80 kg)			
Week	**Dose (per 250-mL bag)**	**Initial infusion rate**	**Subsequent infusion rate†**
Week 1 (split dose infusion)			
Week 1 day 1	350 mg	50 mL/hr	75 mL/hr
Week 1 day 2	1050 mg	35 mL/hr	50 mL/hr
Week 2	1400 mg	65 mL/hr	
Week 3	1400 mg	85 mL/hr	
Subsequent weeks*	1400 mg	125 mL/hr	

*After week 4, patients are dosed every 2 weeks.
†Increase the initial infusion rate to the subsequent infusion rate after 2 hours in the absence of IRRs.
IRR, infusion-related reaction.
Amivantamab. Package insert. Janssen Biotech, Inc; 2021.

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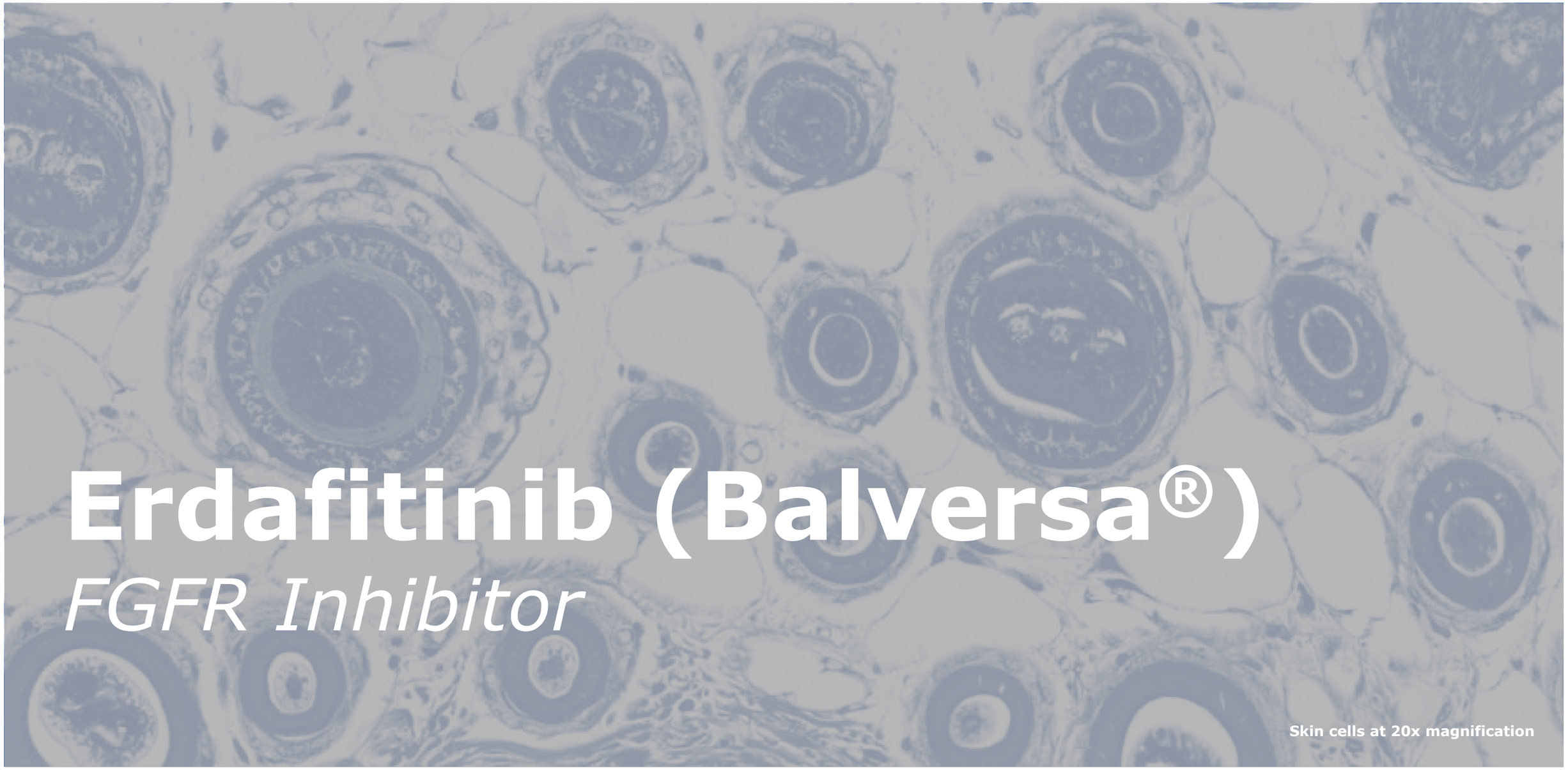
Erdafitinib (Balversa®)

FGFR Inhibitor



Skin cells at 20x magnification

Bladder Cancer: High Unmet Need Across Stages of Disease – once patients progress beyond MIBC, prognosis is poor

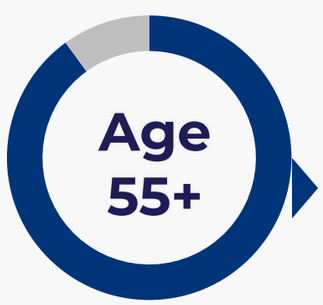
A global annual average of:

550,000
New cases

200,000
Deaths

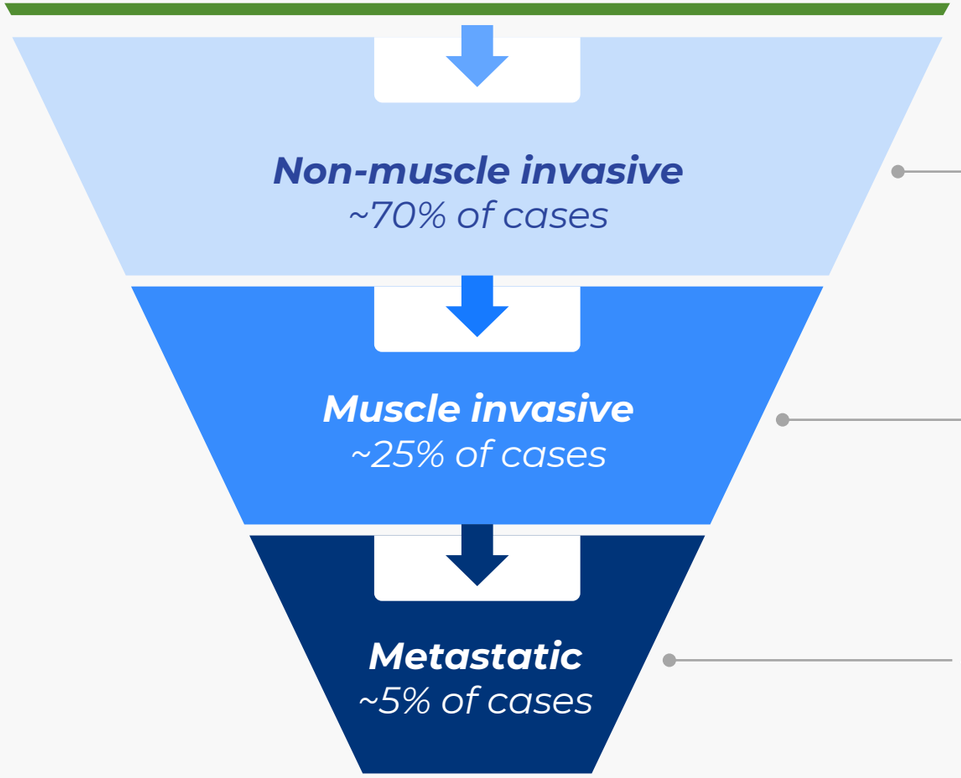
3X More common in men than women

73
Median age at diagnosis



90%
diagnosed at age 55+

Bladder cancer stage at diagnosis



	FGFR rate	5-Year survival
Non-muscle invasive (~70% of cases)	~40%	80%+
Muscle invasive (~25% of cases)	~30%	50%
Metastatic (~5% of cases)	~20%	5%

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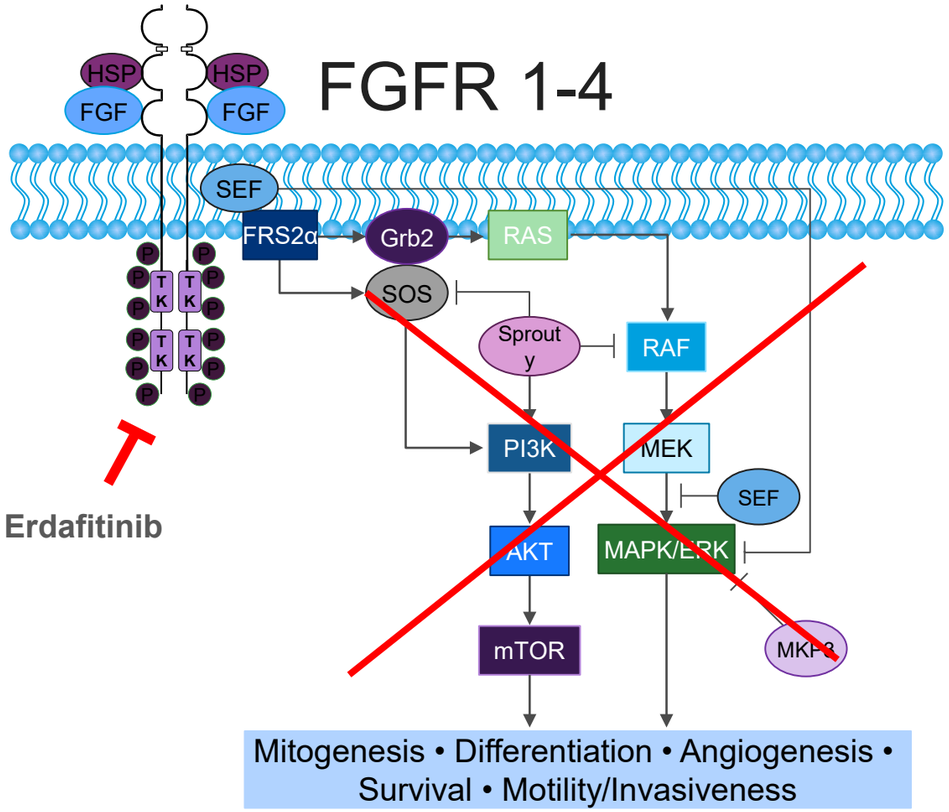
Erdafitinib - BLC 2001 UC

Mode of Action



Pivotal study results (FDA) – Objective response rate

Response Characteristic	All Patients (N=99)	[95% CI]
Response per investigator assessment[a,b], n (%)		
ORR	**40** (40.4)	[30.7-50.1]
Complete response	3 (3.0)	
Partial response	37 (37.4)	
Stable disease	**39** (39.4)	
Progressive disease	18 (18.2)	
Median time to response	1.4 months	
Median duration of response	5.6 months	[4.2-7.2]
ORR among patient subgroups, n (%)		
Chemo-naïve vs progressed/relapsed after chemo	5/12 (41.7) vs 35/87 (40.2)	
With vs without visceral metastases	30/78 (38.5) vs 10/21 (47.6)	

[a] Confirmed with second scan at least 6 weeks following the initial observation of response.
[b] Response in 2 patients was unknown.

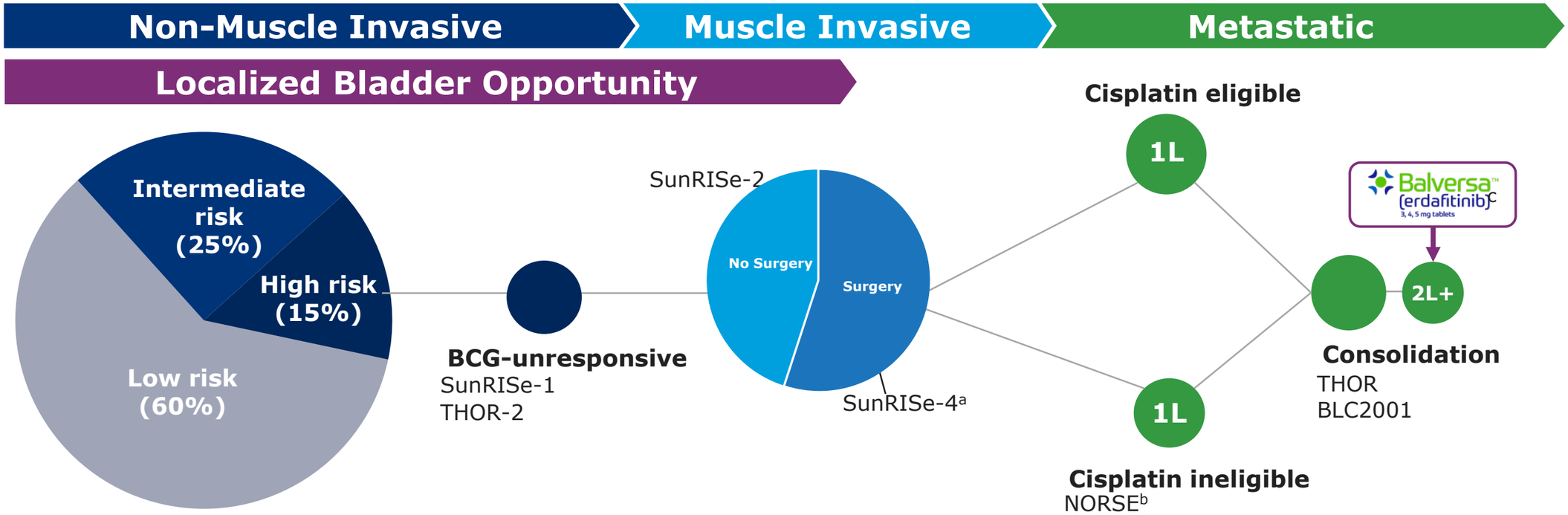
21.2% of patients remain on study treatment after 11 months of follow-up

Study met the primary objective

Clegg NJ, et al. Cancer Res. 2012;72:1494-1503.
Corn PG, et al. Clin Cancer Res. 2013;19:5856-5866.

1. Loriot Y, et al. *N Engl J Med*. 2019:381:338-348.
2. Siefker-Radtke A, et al. Presented at the ASCO Annual Meeting. June 1-5, 2018, Chicago, IL. Abstract 4503.

Erdafitinib – klinisches Entwicklungsprogramm



Note: size of bubbles roughly represents the proportion of eligible patients.
[a]SunRISe-4 is a non-registrational neoadjuvant study; [b]Study is non-registrational. An investigational treatment associated with the NORSE study has been approved for sale to the public. See https://clinicaltrials.gov/ct2/show/NCT03825484 for more information; [c]Approved indication.
1L, first-line; 2L+, second-line or higher; BCG, Bacillus Calmette-Guerin.

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Recruiting Study Schemas Overview

Study	NCT Identifier	Phase	Compound	Disease
THOR	NCT03390504	III	Erdafitinib (FGFR inhibitor)	Advanced UC
SunRISe-2	NCT04658862	III	TAR-200 (GemRIS™) + cetrelimab (anti-PD-1 mAb)	MIBC
SunRISe-3	NCT05714202*	III	TAR-200 GemRIS™) + ceterlimab (anti-PD-1 mAb)	NMIBC
SunRISe-1	NCT04640623	IIb	TAR-200 (GemRIS™) + cetrelimab (anti-PD-1 mAb)	NMIBC
SunRISe-4	NCT04919512	II	TAR-200 (GemRIS™) + cetrelimab (anti-PD-1 mAb)	MIBC
LUC1001	NCT02908906	I/II	Cetrelimab (anti-PD-1 mAb)	Advanced solid tumors
BLC1003	NCT05316155	I	TAR-210 (pan-FGFR TKI)	NMIBC/MIBC

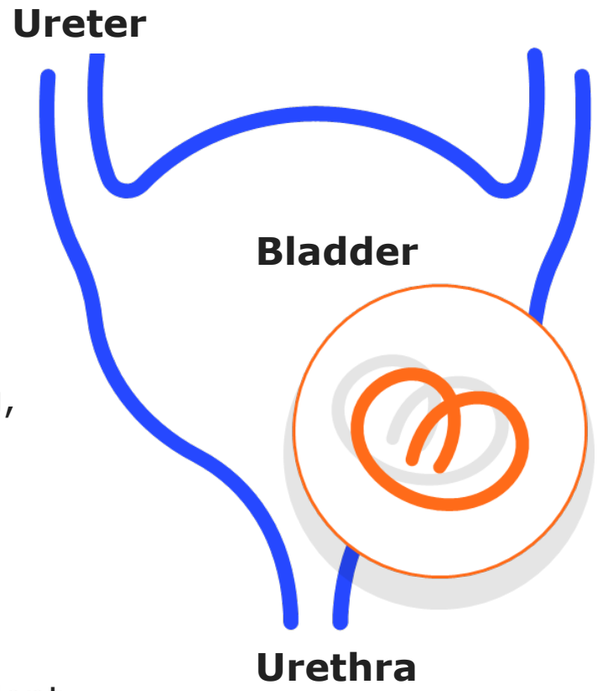
Please refer to disclaimer slide.
*Recruiting soon.

EGFR, epidermal growth factor receptor; FGFR, fibroblast growth factor receptor; mAb, monoclonal antibody; MIBC, muscle invasive bladder cancer; NMIBC, non-muscle invasive bladder cancer; PD-1, programmed cell death protein 1; UC, urothelial cancer; TKI, tyrosine kinase inhibitor.

The TARIS System®

TARIS System®: Providing Continuous Release of Chemotherapy for Patients with Bladder Cancer

- The **TARIS system®** has been designed by TARIS Biomedical® to continuously release chemotherapy into the bladder over time.
- This is a **small, flexible wire** within the **silicone tubing** which maintains a **pretzel shape** once inside the bladder
  - Placed in the bladder as a straight, soft tube with an inserter (a soft, thin tube, similar to a urinary catheter)
  - Curls into a pretzel shape after it is released into the bladder
  - The osmotic tablets within the device modulate chemotherapy release from the internal reservoir
  - The patient generally does not feel the device once it lies within the bladder
  - There are no limitations to patient activity while the device is indwelling, although the chemotherapy load may cause some dysuria or burning with urination.
- Insertion and removal can be performed by a urologist in clinic using existing procedures (catheterization, cystoscope); the TARIS system® device is inserted under local anesthesia.
- This is designed to be freely moving, retained in the bladder with excellent tolerability; the dose and duration can be tailored to specific diseases.



Janssen Global. Janssen Oncology Strengthens Disease Interception Focus with TARIS' Unique Delivery System. Published August 14, 2020. www.janssen.com/oncology/janssen-oncology-strengthens-disease-interception-focus-taris-unique-delivery-system. (Accessed March 7, 2023).

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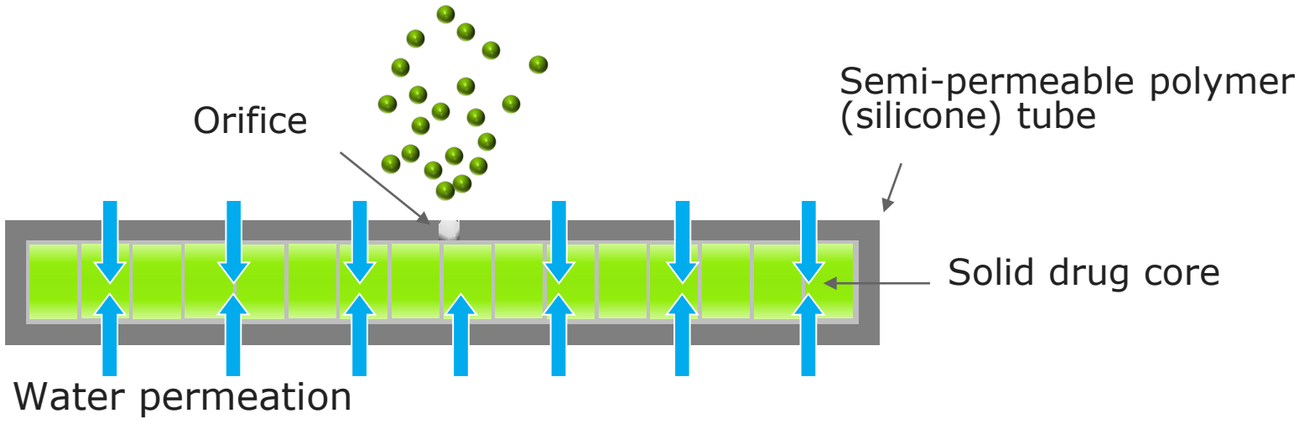
TARIS System®: Enabling the Creation of Localized Regimens with Tailorable Dosing

Example of delivery: Osmotic engine



- Osmotic pump modulates drug release from internal reservoir.
- Dose and duration tailored to specific disease states.
- **Optimal dosing maximizes intracellular drug potency**.

Grimberg DC, et al. Eur Urol Focus 2019;6:620–2.