**Sprecher**
Prof. Dr. Peter Dreger
Universitätsklinikum Heidelberg
Medizinische Klinik V
INF 410, 69120 Heidelberg
Tel. +49 (0) 6221-56 8030
Fax +49 (0) 6221-56 6511
info@dag-hszt.de

**Stellvertretender Sprecher**
Prof. Dr. W. Bethge, Tübingen

**Sekretär**
Prof. Dr. P.-G. Schlegel, Würzburg

**Schatzmeister**
Prof. Dr. G. Kobbe, Düsseldorf

**Vorstandsmitglieder**
Prof. Dr. F. Ayuk, Hamburg
PD Dr. G. Bug, Frankfurt/M
Prof. Dr. J. Schetelig, Dresden
Prof. Dr. M. Stelljes, Münster
Prof. Dr. E.M. Wagner-Drouet, Mainz

**Vorstandssekretariat**
A. Blömeke
CSI Hamburg GmbH
Goernestr. 30, 20249 Hamburg
Tel. +49 (0) 40-30770300
Fax +49 (0) 40-30770301
info@dag-hszt.de

Heidelberg, 18.03.2024

Mitglieder
DAG-HSZT

**Zelltherapiediskussion mit dem KCO am 18.03.2024**

Liebe Kolleg*innen,

bei der 3. Gesprächsrunde 2024 mit dem KCO zur Indikationsstellung von Zelltherapien waren als Repräsentanten der DAG-HSZT vertreten Peter Dreger, Matthias Stelljes und Eva Wagner; Francis Ayuk und Gerald Wulf für die GLA; Christof Scheid und Hans Salwender für die GMMG; sowie Axel Heyll, Eva Hilgenfeld, Anja Knödler, und Ekkehard Ost für das KC Onkologie.

Hauptthema waren die in Kürze zu erwartenden Zulassungserweiterungen für Abecma (3L) und Carvykty (2L, Einzelheiten s. Anlage 1). A Heyll begann mit einer kurzen Übersicht über BCMA-adressierende Immuntherapeutika beim Myelom. Schlussfolgerung war, dass bei CART-geeigneten Patienten und Erfüllung der Zulassungsanforderungen an die Vorbehandlung BCMA-CARTs den Vorzug vor BCMA-BiTEs, aber auch rein pharmakologischen Therapien erhalten sollten. Essenziell sei in jedem Fall die frühzeitige Abstimmung der Therapiestrategie im Tumorboard der CART-Zentren (Anlage 1).

In einer komplementären Darstellung bestätigte C Scheid diesen Algorithmus aus Sicht der Anwender, wobei er einige sich aus den spezifischen Anwendungsvoraussetzungen ergebende Fallstricke aufzeigte (Anlage 2). Er betonte, dass durch Verlagerung der CART-Indikation in frühe Linien sich nicht nur die mutmaßliche Wirksamkeit der CARTs, sondern auch die Bridging-Optionen verbessern dürften.

Bei der nächsten Gesprächsrunde am 22.04.2024 soll das Thema CARTs bei HIV im Mittelpunkt stehen.

Herzliche Grüße

Peter Dreger

Medizinischer Dienst

Kompetenz-Centrum Onkologie

# CAR-T-Zellen beim multiplen Myelom

## CAR-T-Zell-Kolloquium mit DAG-HSZT

Düsseldorf, den 19. März 2024

Prof. Dr. med. Axel Heyll, Leiter des Kompetenz Centrums Onkologie der Medizinischen Dienste

Kompetenz-Centrum Onkologie

## Offenlegung Interessenskonflikte

**1. Anstellungsverhältnis oder Führungsposition** **Leiter des KC Onkologie der Medizinischen Dienste, angestellt beim MD Nordrhein**

**2. Beratungs- bzw. Gutachtertätigkeit** **Für GKV Gutachten und Beratung als Arzt des Medizinischen Dienstes entsprechend SGB V**

**3. Besitz von Geschäftsanteilen, Aktien oder Fonds** **Nein**

**4. Patent, Urheberrecht, Verkaufslizenz** **Nein**

**5. Honorare** **Nein**

**6. Finanzierung wissenschaftlicher Untersuchungen** **Nein**

**7. Andere finanzielle Beziehungen** **Nein**

**8. Immaterielle Interessenkonflikte** **Nein**

# Zugelassene CAR-T-Zell-Präparate

Kompetenz-Centrum Onkologie

- Idecabtagen vicleucel (Abecma®)
  - R-r multiples Myelom nach mindestens **zwei** vorausgegangenen Therapien einschließlich IMID, Proteasominhibitor, Anti-CD38 AK und Progress unter letzter Therapie
- Ciltacabtagen autoleucel (Carvikty®)
  - R-r multiples Myelom nach mindestens **einer** vorausgegangenen Therapie einschließlich IMID und Proteasominhibitor, Progress unter letzter Therapie und refraktär für Lenalidomid

# Zugelassene bispezifische Antikörper

Kompetenz-Centrum Onkologie

- Teclistamab (Tecvayli®), subkutane Applikation, BCMA- und CD3-gerichtet
  - R-r multiples Myelom nach mindestens 3 Therapien, darunter IMID, Proteasominhibitor und CD38-AK und Progress unter letzter Therapie
- Elranatamab (ELREFIXO®), subkutane Applikation, BCMA- und CD3-gerichtet
  - R-r multiples Myelom nach mindestens 3 Therapien, darunter IMID, Proteasominhibitor und CD38-AK und Progress unter letzter Therapie
- Talquetamab (Talevy®), subkutane Applikation, GPRC5D- und CD3-gerichtet
  - R-r multiples Myelom nach mindestens 3 Therapien, darunter IMID, Proteasominhibitor und CD38-AK und Progress unter letzter Therapie

| | Teclistamab MajesTEC-1 Phase 1/2 N = 165 | Update | Elranatamab MagnetisMM-1 Phase-1 N = 55 (88) | Elranatamab MagnetisMM-3 Phase-2 N = 123 | Talquetamab MonumenTAL-1 Phase-1 N = 232 | Update Phase-2 N = 288 |
|---|---|---|---|---|---|---|
| Epitop | BCMA | BCMA | BCMA | BCMA | GPRC5D | GPRC5D |
| Verabreichung | s.c. (QW, Q2W) | s.c. (QW, Q2W) | i.v./s.c. | s.c. (QW, Q2W) | (i.v.) s.c. (2 Dosierungen) | s.c. (QW, Q2W) |
| Stationär initial „step-up“ | Studie ja, Nicht vorgeschrieben | | | Studie: ja | Studie ja, Nicht vorgeschrieben | |
| ECOG; ≥ 1 | 0 – 1/66,7 % | | ≥ 2 (9,1 %) | 1: 57,7 %/2: 5,7 % | ? | ? |
| Alter, Median | 64 (33 – 84) | | 64 (42 – 80) | 68 (36 – 89) | 64 (39 – 84) | |
| Anzahl Vortherapien | 5 | 5 | 5 | 5 | 6 | 5 - 6 |
| Triple refraktär | 77,6 % | 78 % | 90,9 % | 96,7 % | 75 % | 74 %/69 % |
| Follow-up Monate | 14,1 | 22 | 12 | 14,7 | 11,7/ 4,2 | 14,9/8,6 |
| ORR | 63 % | | 63,6 % | 61 % | 70 %/64 % | 74 %/ 73 % |
| ≥ CR | 39,4 | 43 % | 38,2 % | 35 % | 23 %/ 22 % | |
| Med. PFS Monate | 11,3 | 12,5 | 11,8 | Not reached | | 7,5 /11,9 |
| Med. OS Monate | 18,3 | 21,9 | 21.2 | Not reached | | |
| CRS; ≥ Grad 3 | 72,1 %/ 0,6 % | | 0 % | 57,7 %/ 0 % | 77 bzw. 80 %/ 1 Pat. s.c. | 79 bzw.75 % |
| ICANS; ≥ Grad 3 | 3 %/ 0 % | | 0 % | 3,4 % / 0 % | Grad 3: 0 % bei s.c. | 11 % gesamt |
| ORR bei anti-BCMA-Vortherapie | | 40 %<br>52,5 % (EPAR) | 26,3 % der Pat.:<br>53.8 % | 45,3 %<br>(Vortherapien 7) | | 51 Pat. „T-cell-redirection“: 63%, PFS 5,1 Mo |

**Table 1. Baseline Characteristics and Outcomes in Specific Populations**

| BASELINE CHARACTERISTICS | N (%) – total 102 |
|---|---|
| Male | 47 (46%) |
| Age, years, median (range) | 66.5 (35–87) |
| IgG subtype | 54 (53%) |
| RISS (Revised International Staging System)- III | 25 (25%) |
| High risk cytogenetics* | 55 (54%) |
| Extramedullary disease | 45 (44%) |
| Prior lines of therapy (LOT) (median, range) | 6 (4–17) |
| Refractory to proteasome inhibitor | 102 (100%) |
| Refractory to Immunomodulatory drugs | 102 (100%) |
| Refractory to anti-CD38 monoclonal antibody | 102 (100%) |
| Prior Autologous stem cell transplant | 60 (59%) |
| Double refractory † | 94 (92%) |
| Triple refractory ‡ | 94 (92%) |
| Penta refractory § | 68 (67%) |
| BDT refractory | 56 (55%) |
| **EFFICACY OUTCOMES** | |
| Overall Response Rate (n=102) | 65 (64% |
| • Partial response (PR) | 18 (18%) |
| • Very good partial response (VGPR) | 18 (18%) |
| • Stringent complete response (sCR)/CR | 29 (28%) |
| | **Overall Response Rate** |
| Age >70 (n=33) | 23 (70%) |
| Non-Hispanic Black (n=25) | 17 (68%) |
| Ineligible for MajesTEC-1 trial (n=83) | 49 (59%) |
| R-ISS III (n=25) | 13 (52%) |
| High-risk cytogenetics (n=55) | 34 (62%) |
| EMD (n=44) | 20 (45%) |
| CrCl < 40 mL/min (n=13) | 7 (54%) |
| Four or less prior LOT (n=23) | 18 (78%) |
| More than four prior LOT (n=79) | 47 (59%) |
| Triple Refractory (n=94) | 58 (62%) |
| Penta Refractory (n=68) | 45 (66%) |
| BDT refractory (n=56) | 32 (57%) |
| • Prior belantamab mafodotin (n=23) | 15 (65%) |
| • Prior BCMA directed CAR T (n=42) | 25 (60%) |
| • ≥ 2 prior BCMA directed therapies (n=13) | 9 (69%) |

* High-risk cytogenetics: deletion 17, t(4;14), t(14;16), t(14;20) and gain/amplification of 1q
† Double refractory: refractory to at least 1 IMiD, and at least 1 PI
‡ Triple refractory: refractory to at least 1 IMiD, at least one PI and at least 1 anti-CD38 mAb
§ Penta refractory: refractory to at least 2 IMiD, at least 2 PI and at least 1 anti-CD38 mAb.

Dima D et al., Real-World Safety and Efficacy of Teclistamab for Patients with Heavily Pretreated Relapsed-Refractory Multiple Myeloma,
Abstract No. 91, ASH 2023

Kompetenz-Centrum Onkologie

| | Intended SOC, N=22 | MajesTEC-1, N=165 |
|---|---|---|
| Median age, yrs | 66 (48-81) | 64 (33-84) |
| ECOG PS 0 or 1 | 20 (91%) | 165 (100%) |
| Extramedullary disease | 3 (14%) | 28 (17%) |
| High marrow burden | 6 (27%) | 18 (11%) |
| High-risk cytogenetics | 11 (50%) | 38 (26%) |
| Median prior regimens (range) | 8 (5-13) | 5 (2-14) |
| Penta-refractory disease | 11 (50%) | 50 (30%) |
| Grade ≥ 3 CRS and ICANS | 0%/5% | 0.6%/3% |
| Prior BCMA-TT | | |
| CAR-T | 15 (68%) | 0% |
| ADC | 2 (9%) | 0% |
| Both CAR-T and ADC | 5 (23%) | 0% |
| Best ORR/≥CR | 63%/36% | 63%/39% |

Grajales-Cruz AF et al.., Real-World Safety and Efficacy of Teclistamab for Patients with r-r Multiple Myeloma and prior BCMA-directed therapy,
Abstract No. 3351, ASH 2023

# Vergleich PFS und OS ab der 4. Linie

Kompetenz-Centrum Onkologie

| Medikament | Ide-cel | Clita-cel | Teclistamab | Elranatamab | Talquetamab |
|---|---|---|---|---|---|
| Medianes PFS (Monate) | 8,8 | > 27 | 12,5 | 11,8 | 11,9 |
| Medianes OS (Monate | 19,4 | > 27 | 21,9 | 21,2 | ? |

**Mögliche Therapiestrategie**

- Prüfung der Option einer zellulären Therapie nach 2 bis 4 Linien in Abhängigkeit vom Verlauf
  - Bei Entscheidung zur zellulären Therapie klare Strategie festlegen!
- Prüfung der Eignung der/es Pat. für eine CAR-T-Zell-Therapie
  - Günstige Prognosefaktoren für CAR-T-Zellen: zunächst Ciltacel, dann ggf. bispez. AK?
  - Ungünstige Prognosefaktoren: Bispez. AK, ggf. zunächst BCMA-gerichtet, dann GRPC5D-gerichtet?
- Vermeiden: Gabe von bispez. AK vor CAR-T-Zellen, besonders BCMA-gerichtet!

# Prüfung der Eignung der/s Pat. für CAR-T-Zellen

Kompetenz-Centrum Onkologie

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY driving innovation in oncology

SPECIAL ARTICLE

## Management of adults and children receiving CAR T-cell therapy: 2021 best practice recommendations of the European Society for Blood and Marrow Transplantation (EBMT) and the Joint Accreditation Committee of ISCT and EBMT (JACIE) and the European Haematology Association (EHA)

P. J. Hayden[1†], C. Roddie[2,3*†], P. Bader[4], G. W. Basak[5], H. Bonig[6], C. Bonini[7], C. Chabannon[8], F. Ciceri[9], S. Corbacioglu[10], R. Ellard[11], F. Sanchez-Guijo[12], U. Jäger[13], M. Hildebrandt[14], M. Hudecek[15], M. J. Kersten[16], U. Köhl[17,18], J. Kuball[19], S. Mielke[20], M. Mohty[21], J. Murray[22], A. Nagler[23], J. Rees[3,24], C. Rioufol[25], R. Saccardi[26], J. A. Snowden[27], J. Styczynski[28], M. Subklewe[29], C. Thieblemont[30], M. Topp[15], Á. U. Ispizua[31], D. Chen[3,32], R. Vrhovac[33], J. G. Gribben[32], N. Kröger[34], H. Einsele[15] & I. Yakoub-Agha[35]

blood Regular Article

Kompetenz-Centrum Onkologie

IMMUNOBIOLOGY AND IMMUNOTHERAPY

# CAR-HEMATOTOX: a model for CAR T-cell–related hematologic toxicity in relapsed/refractory large B-cell lymphoma

Kai Rejeski,[1-3] Ariel Perez,[4] Pierre Sesques,[5] Eva Hoster,[1,6] Carolina Berger,[7] Liv Jentzsch,[8] Dimitrios Mougiakakos,[9] Lisa Frölich,[1,3] Josephine Ackermann,[1] Veit Bücklein,[1,2] Viktoria Blumenberg,[1,2] Christian Schmidt,[1] Laurent Jallades,[5] Boris Fehse,[7] Christoph Faul,[8] Philipp Karschnia,[3,10] Oliver Weigert,[1,3] Martin Dreyling,[1] Frederick L. Locke,[4] Michael von Bergwelt-Baildon,[1,3] Andreas Mackensen,[9] Wolfgang Bethge,[8] Francis Ayuk,[7] Emmanuel Bachy,[5] Gilles Salles,[5] Michael D. Jain,[4] and Marion Subklewe[1-3]

[1]Department of Medicine III, University Hospital, Ludwig Maximilian University (LMU) Munich, Munich, Germany; [2]Laboratory for Translational Cancer Immunology, LMU Gene Center, Munich, Germany; [3]German Cancer Consortium, Munich Site, and German Cancer Research Center, Heidelberg, Germany; [4]Department of Blood and Marrow Transplant and Cellular Immunotherapy, Moffitt Cancer Center, Tampa, FL; [5]Hospices Civils de Lyon, Université Claude Bernard Lyon 1, INSERM 1052, Pierre-Bénite, France; [6]Institute for Medical Informatics, Biometry and Epidemiology, LMU Munich, Munich, Germany; [7]Department of Hematology, Oncology and Pulmonology, University Hospital Hamburg-Eppendorf, Hamburg, Germany; [8]Department of Hematology, Oncology, Immunology and Rheumatology, University Hospital Tübingen, Tübingen, Germany; [9]Department of Internal Medicine 5, Hematology and Oncology, University Hospital of Erlangen, Erlangen, Germany; and [10]Department of Neurosurgery, University Hospital, LMU Munich, Munich, Germany

## Prognosefaktoren für CAR-T-Zellen zunächst validiert an CD19 CAR-T-Zellen

| Baseline Features | 0 Point | 1 Point | 2 Points |
|---|---|---|---|
| Platelet Count | > 175,000/µl | 75,000 – 175,000/µl | < 75,000/µl |
| Absolute Neutrophil Count (ANC) | > 1200/µl | < 1200/µl | - |
| Hemoglobin | > 9.0 g/dl | < 9.0 g/dl | - |
| C-reactive protein (CRP) | < 3.0 mg/dl | > 3.0 mg/dl | - |
| Ferritin | < 650 ng/ml | 650 – 2000 ng/ml | > 2000 ng/ml |
| Low: 0-1 | High: ≥ 2 | | |

**Figure 4. CAR-HEMATOTOX.** Determined before lymphodepletion, the score comprises 5 markers of hematotoxicity with additional weighting of the baseline platelet count and ferritin levels. The score discriminates between a high (CAR-HEMATOTOX score ≥2) and low (CAR-HEMATOTOX score 0-1) risk for hematotoxicity.

Rejeski *et al.*
*Journal of Hematology & Oncology* (2023) 16:88
https://doi.org/10.1186/s13045-023-01465-x

Journal of
Hematology & Oncology

**RESEARCH** **Open Access**

# The CAR-HEMATOTOX score as a prognostic model of toxicity and response in patients receiving BCMA-directed CAR-T for relapsed/refractory multiple myeloma

Kai Rejeski[1,2,3,4*†], Doris K. Hansen[5†], Radhika Bansal[6], Pierre Sesques[7], Sikander Ailawadhi[8], Jennifer M. Logue[5], Eva Bräunlein[9], David M. Cordas dos Santos[1,3], Ciara L. Freeman[5], Melissa Alsina[5], Sebastian Theurich[1,3], Yucai Wang[6], Angela M. Krackhardt[3,4,9,10], Frederick L. Locke[5], Emmanuel Bachy[7], Michael D. Jain[5], Yi Lin[6†] and Marion Subklewe[1,2,3,4†]

Kompetenz-Centrum Onkologie

German Lymphoma Alliance

AKTUELLES | STUDIEN | ARBEITSGRUPPEN | REGISTER | FÜR PATIENTEN | ÜBER UNS | LOGIN

*(5): e004475.*

**Calculator**

Here you can calculate the CAR-HEMATOTOX score and the resulting risk group (high versus low). By using this calculator, you accept that the GLA does not assume any liability.

| | |
|---|---|
| Platelet Count | please select... |
| Absolute Neutrophil Count (ANC) | please select... |
| Hemoglobin | please select... |
| C-reactive protein (CRP) | please select... |
| Ferritin | please select... |

CAR-HEMATOTOX score ---

**Please select input...**

Spenden | Mitglied werden | Studie einreichen | Scores

# Mögliche Therapiestrategie

Kompetenz-Centrum Onkologie

1. Frühzeitige Entscheidung über optimale Art der zellulären Therapie
   - Nach 1 – 3 Therapielinien in Abhängigkeit vom Verlauf
   - Keine Vorbehandlung mit bispezifischen AK vor CAR-T-Zell-Gabe, insbesondere nicht BCMA-gerichtet
   - Enge Kooperation mit Zuweisern, frühzeitige Vorstellung am CAR-T-Zell-Zentrum
2. Untersuchung der/es Patientin/en
   - Eignung für CAR-T-Zell-Therapie nach EBMT/EHA-Kriterien
   - Prognosefaktoren nach CAR-HEMATOTOX-Score
     - *Aktuell valide nur für Ide-cel*
3. Entscheidung durch Leukämie-/Lymphomboard über optimale Therapiestrategie
   - Bei Eignung bevorzugt CAR-T-Zellen (i. d. R. Cilta-cel, in einigen Fällen, z. B. aufgrund der geringeren Neurotox. Ide-cel), bei fehlender Eignung bevorzugt BCMA-gerichtete bispezifische AK
   - Künftig attraktive Therapiestrategie bis zu 70 Jahren bei Eignung für CAR-T-Zellen:
     - *1. Linie: Dara-VRD, MEL200 + auto SCT, Dara-VRD-Konsolidierung, Lenalidomid-Erhaltung (ohne Dara!) bis zum Progress*
     - *2. Linie: Bei Progress unter Lena: Cilta-cel*
   - Protokoll des Leukämie-/Lymphom-Boards mit nachvollziehbarer Begründung der Empfehlung

Kompetenz-Centrum Onkologie

# Copyright


- © 2024 Medizinischer Dienst Nordrhein


- Berliner Allee 52, 40212 Düsseldorf
- Telefon: 0211/ 1382-0; Telefax: 0211/ 1382-189
- http://www.md-nordrhein.de; E-Mail: post@md-nordrhein.de



- Alle Rechte vorbehalten, insbesondere das Recht der Vervielfältigung und Verbreitung. Kein Teil des Werkes darf in irgendeiner Form (durch Fotokopie, Mikrofilm oder ein anderes Verfahren) ohne schriftliche Genehmigung des MDK Nordrhein reproduziert oder unter Verwendung elektronischer Systeme verarbeitet, vervielfältigt oder verbreitet werden.

# BCMA-CART in früheren Linien

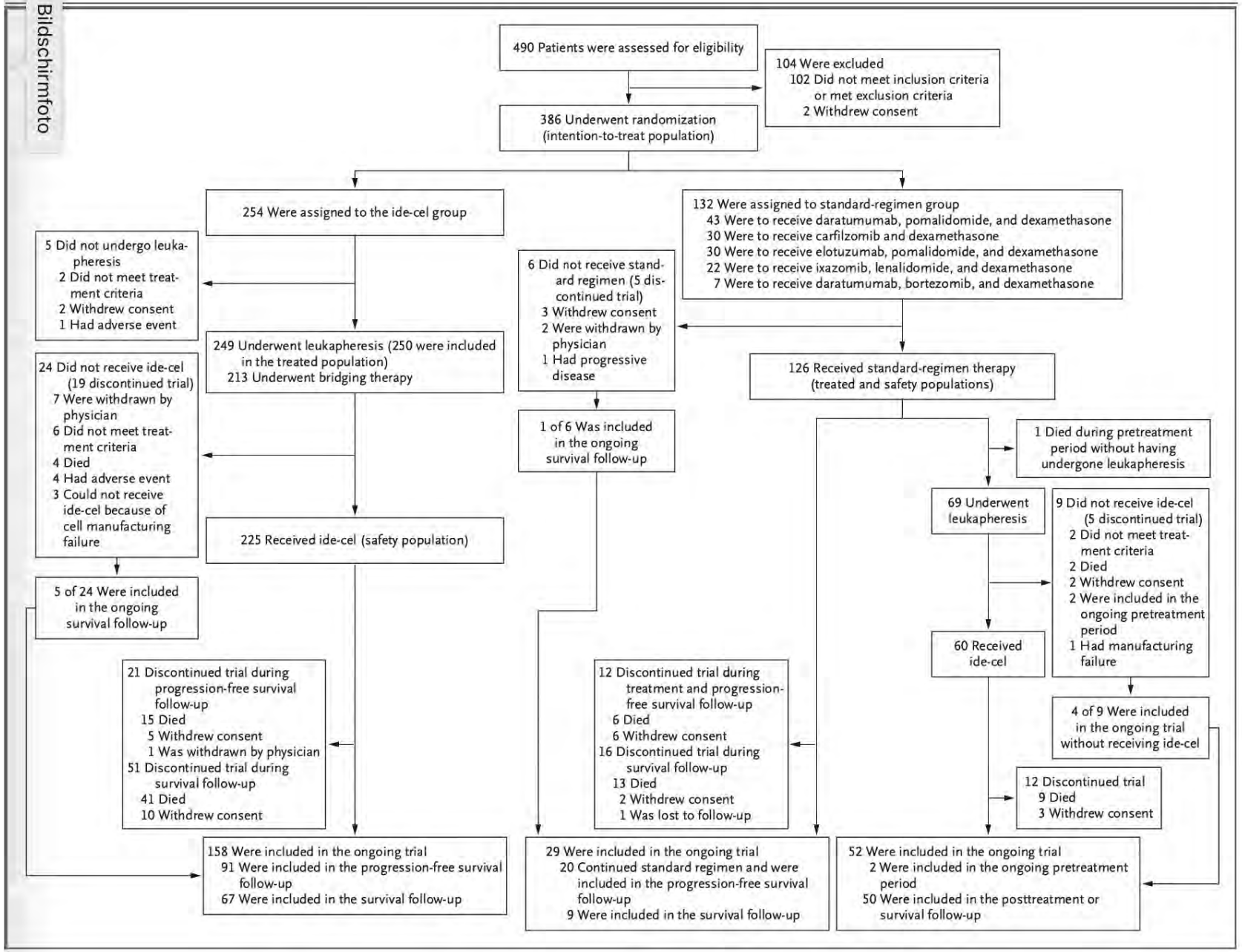
Christof Scheid

18.3.24

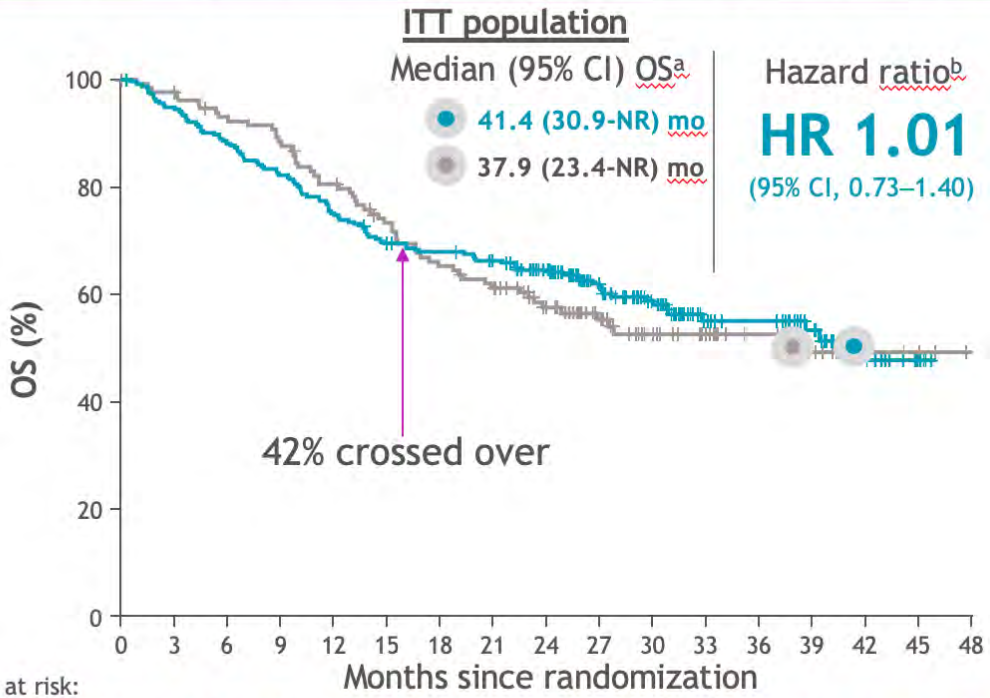
# Neue Indikationserweiterungen

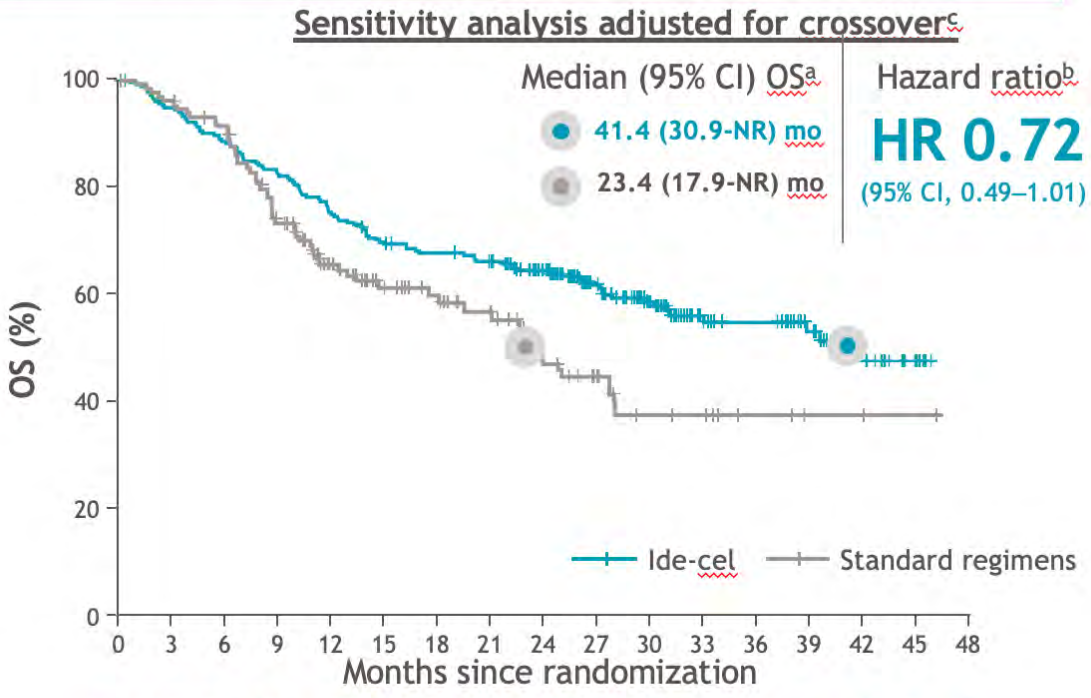
- Abecma is indicated for the treatment of adult patients with relapsed and refractory multiple myeloma who have received at least ~~three~~**two** prior therapies, including an immunomodulatory agent, a proteasome inhibitor and an anti CD38 antibody and have demonstrated disease progression on the last therapy.

Bildschirmfoto



# OS analysis confounded by substantial crossover




Patients at risk:

| | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Ide-cel | 254 | 240 | 223 | 208 | 190 | 175 | 169 | 161 | 143 | 103 | 75 | 48 | 44 | 30 | 13 | 4 | 0 |
| Standard regimens | 132 | 128 | 120 | 114 | 103 | 91 | 81 | 75 | 59 | 45 | 32 | 24 | 18 | 11 | 4 | 3 | 0 |

| | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Ide-cel | 254 | 240 | 223 | 208 | 190 | 175 | 169 | 161 | 143 | 103 | 75 | 48 | 44 | 30 | 13 | 4 | 0 |
| Standard regimens | 132 | 126 | 118 | 93 | 67 | 50 | 42 | 34 | 21 | 14 | 9 | 8 | 4 | 2 | 1 | 1 | 0 |

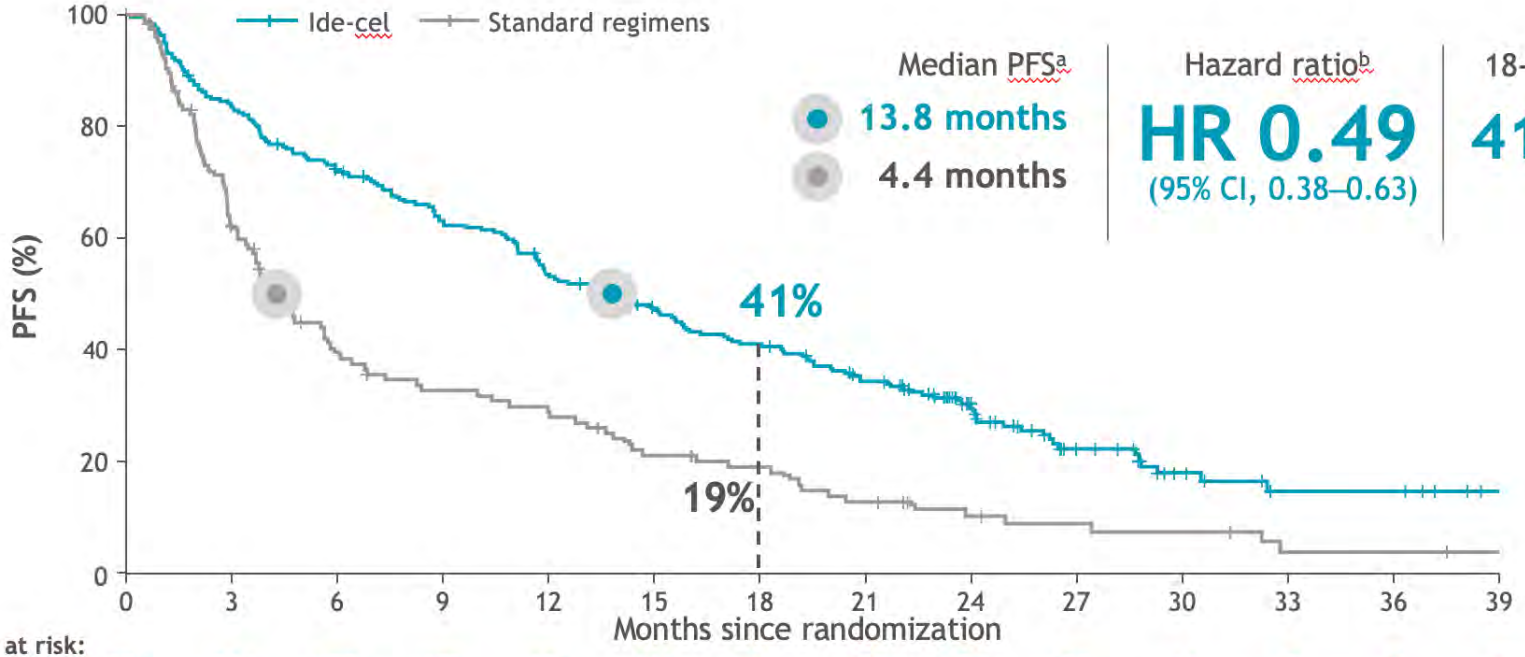
**More than half of patients in standard regimens arm received ide-cel as subsequent therapy upon confirmed PD and the majority received ide-cel within 3-16 months of randomization**

**Prespecified crossover-adjusted analysis shows OS benefit of ide-cel**

Information fraction for OS was 74% (n = 164/222 required events). [a]Based on Kaplan-Meier approach; [b]Stratified HR is based on the univariate Cox proportional hazards model. CI is two-sided and calculated by bootstrap method; [c]Two-stage Weibull model without re-censoring (prespecified analysis).
mo, month; NR, not reached.

Rodríguez-Otero P, et al. ASH 2023 Abstract 1028

# Significant benefit with ide-cel at final PFS analysis (ITT population)




| | Median PFS[a] | Hazard ratio[b] | 18-month PFS rate | |
|---|---|---|---|---|
| Ide-cel | 13.8 months | HR 0.49 (95% CI, 0.38–0.63) | 41% | |
| Standard regimens | 4.4 months | | | 19% |

Patients at risk:

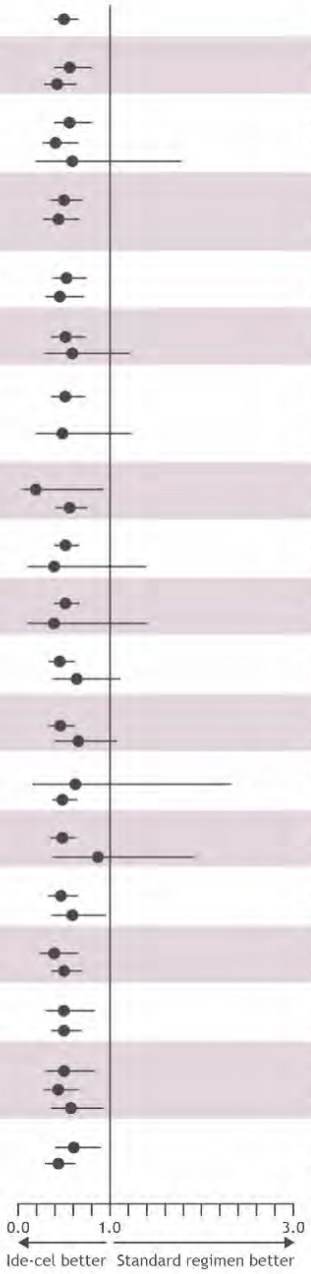
| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Ide-cel | 254 | 206 | 177 | 153 | 131 | 111 | 94 | 77 | 54 | 25 | 14 | 7 | 7 | 2 |
| Standard regimens | 132 | 76 | 43 | 34 | 31 | 21 | 18 | 12 | 9 | 6 | 5 | 3 | 2 | 1 |

PFS was analyzed in the ITT population of all randomized patients in both arms and included early PFS events occurring between randomization and ide-cel infusion. PFS based on IMWG criteria per IRC. [a]Based on Kaplan-Meier approach; [b]Stratified HR based on univariate Cox proportional hazard model. CI is two-sided. IMWG, International Myeloma Working Group.

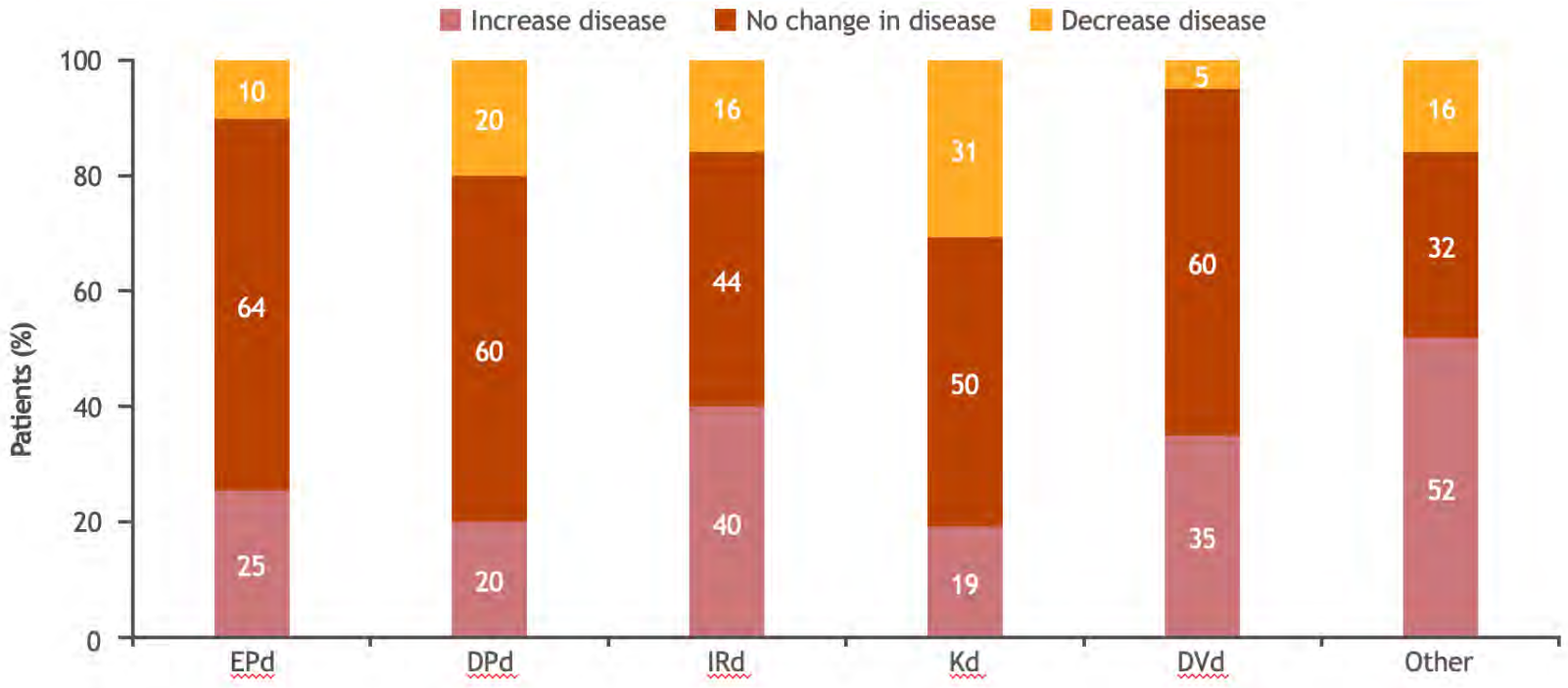
Rodríguez-Otero P, et al. ASH 2023 Abstract 1028

**Figure S1.** Subgroup Analysis of Progression-free Survival.

| | Ide-cel | Standard Regimen | Hazard Ratio (95% CI) | Ide-cel | Standard Regimen |
|---|---|---|---|---|---|
| | *No. of progression or death events/total no.* | | | *Median progression-free survival — months (95% CI)* | |
| **All patients** | 149/254 | 93/132 | 0.51 (0.39-0.66) | 13.3 (11.8-16.1) | 4.4 (3.4-5.9) |
| **Age group** | | | | | |
| <65 | 93/150 | 51/78 | 0.57 (0.40-0.80) | 12.7 (11.1-17.2) | 4.4 (3.2-5.9) |
| ≥65 | 56/104 | 42/54 | 0.43 (0.28-0.64) | 13.3 (11.2-16.6) | 4.7 (3.0-6.9) |
| **Age group** | | | | | |
| <65 | 93/150 | 51/78 | 0.57 (0.40-0.80) | 12.7 (11.1-17.2) | 4.4 (3.2-5.9) |
| 65-74 | 49/92 | 36/45 | 0.42 (0.27-0.65) | 13.3 (11.2-17.4) | 4.2 (3.0-7.5) |
| 75-84 | 7/12 | 6/9 | 0.59 (0.19-1.78) | 13.2 (4.0-NE) | 5.7 (0.9-NE) |
| **Region** | | | | | |
| North America | 84/144 | 60/82 | 0.50 (0.36-0.70) | 13.8 (11.3-19.0) | 4.7 (3.2-6.1) |
| Europe | 63/106 | 32/45 | 0.44 (0.28-0.68) | 12.4 (10.6-16.1) | 3.9 (2.1-6.5) |
| Japan | 2/4 | 1/5 | NC | NE (2.0-NE) | 20.7 (NE-NE) |
| **Sex** | | | | | |
| Male | 92/156 | 55/79 | 0.53 (0.38-0.75) | 13.8 (11.3-17.2) | 4.8 (3.5-7.5) |
| Female | 57/98 | 38/53 | 0.47 (0.31-0.71) | 12.0 (10.2-17.7) | 3.7 (2.8-5.8) |
| **Race** | | | | | |
| White | 101/172 | 54/78 | 0.52 (0.37-0.73) | 13.6 (11.3-17.2) | 4.9 (3.0-8.4) |
| Non-white | 14/28 | 18/27 | 0.59 (0.29-1.22) | 20.3 (11.1-24.0) | 6.9 (3.4-20.7) |
| **Race** | | | | | |
| White | 101/172 | 54/78 | 0.52 (0.37-0.73) | 13.6 (11.3-17.2) | 4.9 (3.0-8.4) |
| Asian | 4/7 | 1/5 | NC | 11.1 (0.8-NE) | 20.7 (NE-NE) |
| African American | 8/18 | 13/18 | 0.50 (0.20-1.23) | 20.3 (8.9-NE) | 6.9 (3.7-22.5) |
| Other | 2/3 | 4/4 | NC | 17.7 (12.7-NE) | 2.7 (1.6-NE) |
| **Ethnicity** | | | | | |
| Hispanic or Latino | 5/11 | 5/8 | 0.21 (0.05-0.93) | 22.6 (1.3-NE) | 6.1 (1.0-NE) |
| Not Hispanic or Latino | 109/188 | 68/98 | 0.56 (0.41-0.76) | 13.8 (11.3-16.2) | 4.9 (3.5-7.5) |
| **Anti-CD38 class refractory** | | | | | |
| Yes | 143/242 | 88/124 | 0.51 (0.39-0.67) | 12.5 (11.3-15.1) | 4.4 (3.2-5.9) |
| No | 6/12 | 5/8 | 0.40 (0.11-1.40) | 19.0 (3.0-NE) | 5.3 (0.6-NE) |
| **Daratumumab refractory** | | | | | |
| Yes | 143/242 | 88/123 | 0.51 (0.39-0.67) | 12.5 (11.3-15.1) | 4.4 (3.2-5.9) |
| No | 6/12 | 5/9 | 0.40 (0.11-1.40) | 19.0 (3.0-NE) | 5.3 (0.6-NE) |
| **Double-class (IMiD agent and PI) refractory** | | | | | |
| Yes | 106/169 | 72/91 | 0.47 (0.34-0.63) | 11.2 (8.7-12.7) | 3.5 (2.9-4.7) |
| No | 43/85 | 21/41 | 0.65 (0.38-1.11) | 17.3 (14.5-22.6) | 12.9 (4.3-NE) |
| **Triple-class refractory*** | | | | | |
| Yes | 103/164 | 70/89 | 0.46 (0.34-0.62) | 11.2 (8.7-12.5) | 3.5 (2.9-4.7) |
| No | 46/90 | 23/43 | 0.65 (0.39-1.09) | 17.3 (14.5-22.6) | 12.9 (4.3-22.5) |
| **Penta-refractory†** | | | | | |
| Yes | 12/15 | 3/5 | 0.63 (0.17-2.33) | 3.9 (2.0-12.0) | 3.0 (1.0-NE) |
| No | 137/239 | 90/127 | 0.49 (0.37-0.64) | 13.8 (11.9-16.6) | 4.7 (3.4-5.9) |
| **Revised ISS stage at baseline** | | | | | |
| I or II | 113/200 | 78/108 | 0.48 (0.36-0.64) | 14.7 (12.1-17.3) | 4.4 (3.2-5.9) |
| III | 27/31 | 8/14 | 0.86 (0.39-1.92) | 5.2 (1.8-7.2) | 3.0 (0.8-6.1) |
| **Tumor burden†** | | | | | |
| <50% | 99/172 | 60/90 | 0.47 (0.34-0.65) | 14.1 (12.0-17.2) | 4.2 (3.2-6.5) |
| ≥50% | 44/71 | 28/34 | 0.60 (0.37-0.97) | 11.0 (7.2-16.2) | 4.9 (2.3-10.1) |
| **Extramedullary plasmacytoma** | | | | | |
| Yes | 48/61 | 28/32 | 0.40 (0.25-0.65) | 7.2 (4.0-11.8) | 2.0 (1.3-3.0) |
| No | 100/192 | 65/100 | 0.51 (0.37-0.70) | 16.1 (12.7-19.8) | 5.9 (4.3-10.1) |
| **Number of prior anti-myeloma regimens** | | | | | |
| 2 | 41/78 | 26/39 | 0.51 (0.31-0.84) | 15.1 (12.7-19.7) | 4.8 (3.2-13.3) |
| 3 or 4 | 108/176 | 67/93 | 0.51 (0.37-0.69) | 12.0 (10.2-14.7) | 4.2 (3.0-5.9) |
| **Number of prior anti-myeloma regimens** | | | | | |
| 2 | 41/78 | 26/39 | 0.51 (0.31-0.84) | 15.1 (12.7-19.7) | 4.8 (3.2-13.3) |
| 3 | 57/95 | 37/49 | 0.44 (0.29-0.68) | 12.5 (10.8-17.7) | 3.2 (2.3-5.7) |
| 4 | 51/81 | 30/44 | 0.58 (0.36-0.92) | 11.2 (7.4-14.1) | 4.9 (3.2-6.9) |
| **High-risk cytogenetic abnormalities** | | | | | |
| Presence | 65/107 | 42/61 | 0.61 (0.41-0.90) | 11.9 (8.0-14.5) | 4.2 (2.4-5.7) |
| Absence or Unknown | 84/147 | 51/71 | 0.44 (0.31-0.63) | 14.7 (12.0-17.7) | 4.8 (3.4-7.5) |



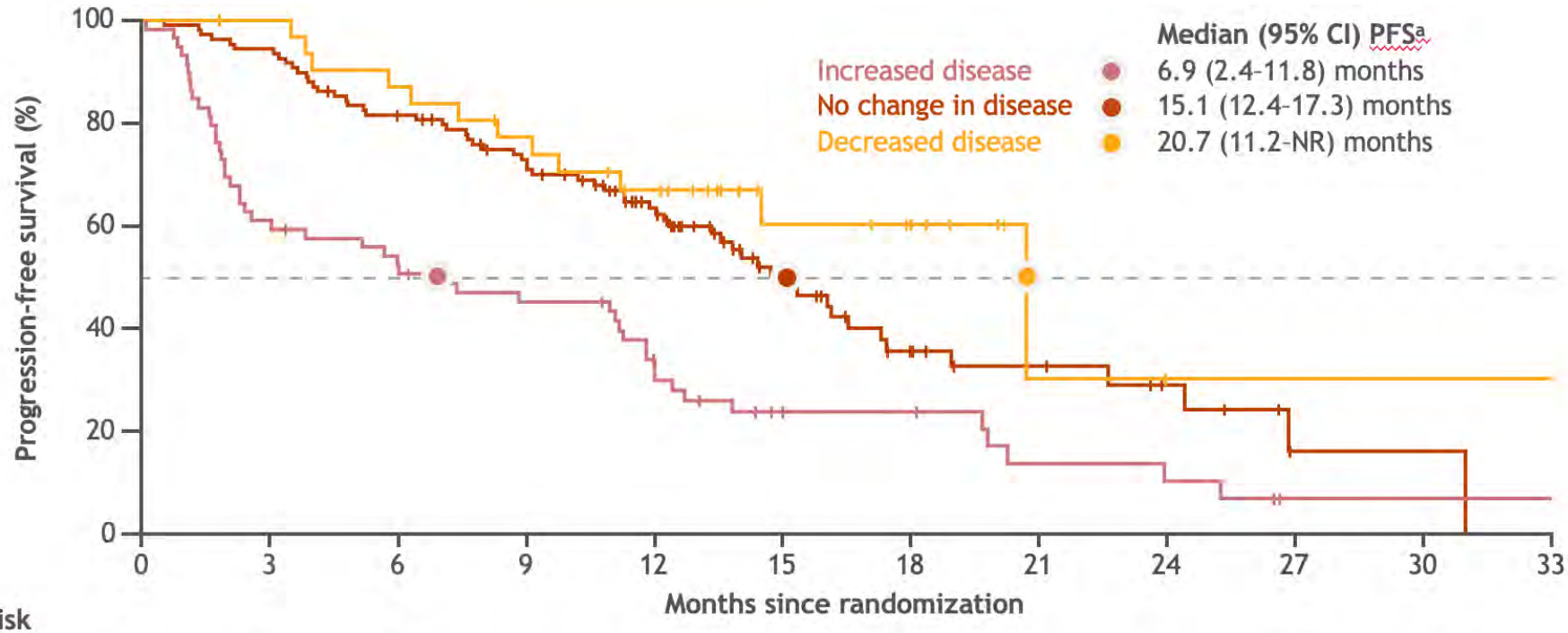
# Figure 3. Change in disease burden by bridging therapy regimen received




Percentages may not sum to 100 due to rounding.

DPd, daratumumab, pomalidomide, and dexamethasone; DVd, daratumumab, bortezomib, and dexamethasone; EPd, elotuzumab, pomalidomide, and dexamethasone; IRd, ixazomib, lenalidomide, and dexamethasone; Kd, carfilzomib and dexamethasone.

# Figure 4. PFS (mITT population)




| Patients at risk | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Increased disease | 59 | 36 | 31 | 25 | 17 | 9 | 8 | 4 | 3 | 0 | 0 | 0 |
| No change in disease | 109 | 103 | 88 | 74 | 54 | 27 | 15 | 10 | 6 | 1 | 1 | 0 |
| Decreased disease | 32 | 31 | 27 | 23 | 18 | 9 | 7 | 1 | 0 | 0 | 0 | 0 |

PFS per IRC based on IMWG criteria according to FDA censoring rules.

[a]Median and 95% CI are based on Kaplan-Meier approach.

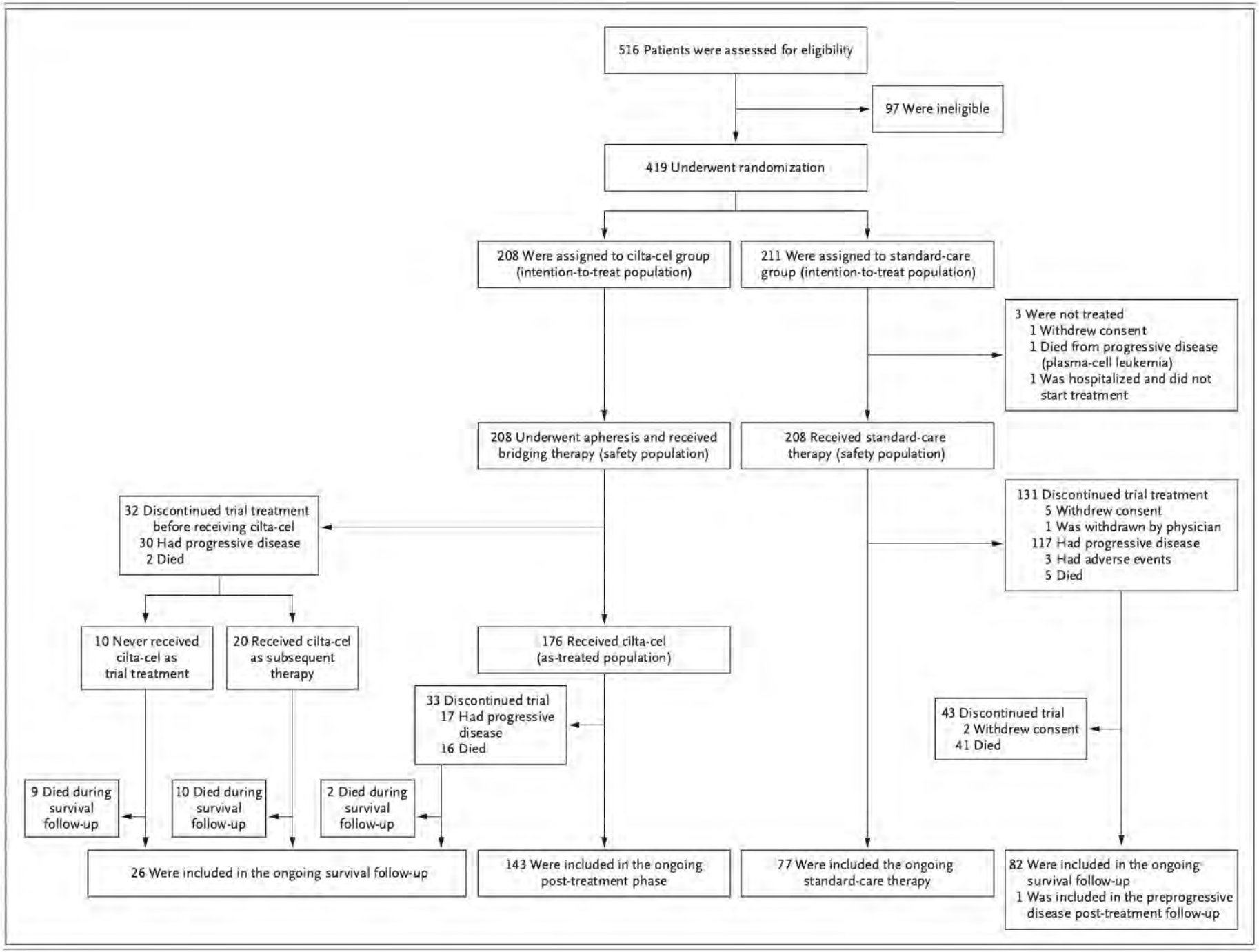
FDA, US Food and Drug Administration; IMWG, International Myeloma Working Group; IRC, independent review committee; NR, not reached; PFS, progression-free survival.

# Abecma

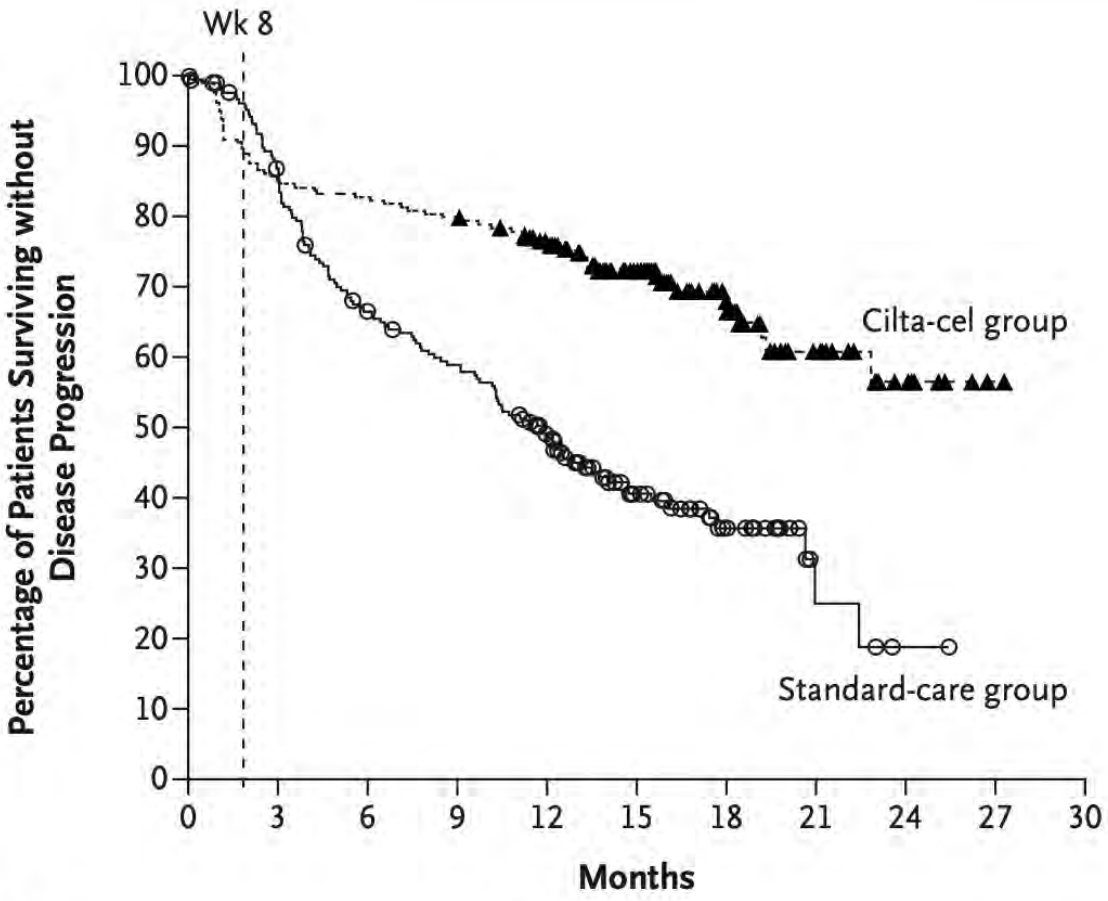
- triple-class exposed and refractory to last line
- z.B. Dara-VTd + PVd oder DRd + PVd
- Brigding: z.B. Kd +-CD38 Ab oder Pd +- CD38 AB nach Kd
- vor CART:
- niedrige Tumorlast
- geringe Inflammation
- wenig Zytopenie

# Neue Indikationserweiterungen

- Carvykti is indicated for the treatment of adult patients with relapsed and refractory multiple myeloma, who have received at least ~~three~~**one** prior therap**y**~~ies~~, including an immunomodulatory agent~~,~~ **and** a proteasome inhibitor ~~and an anti-CD38 antibody and~~, have demonstrated disease progression on the last therapy**, and are refractory to lenalidomide.**



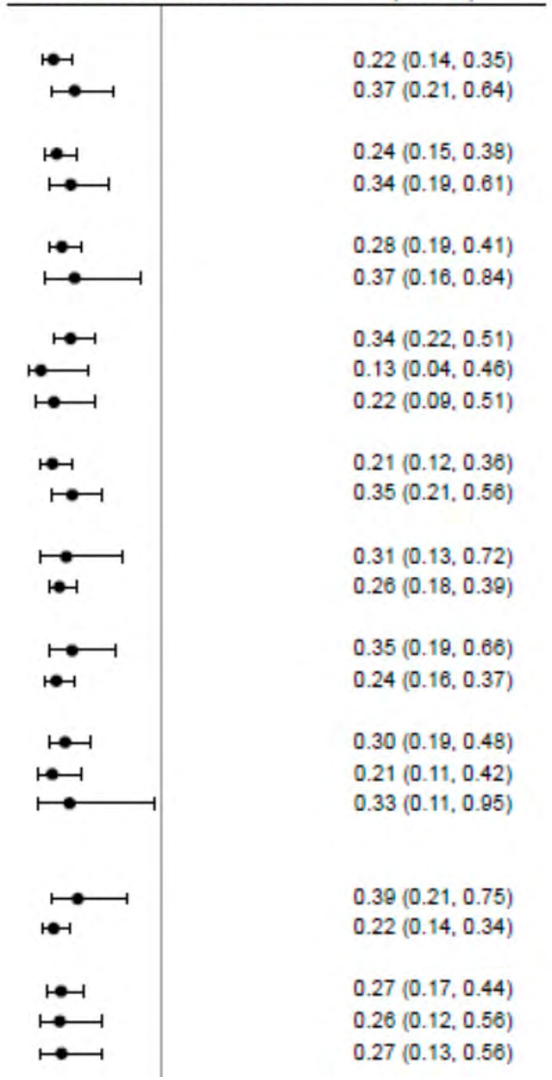

Of the 208 patients who were assigned to receive cilta-cel, 176 (84.6%) actually received the treatment (as- treated population). The remaining 32 patients discontinued trial participation before receiving cilta-cel, mainly because of disease progression during bridging therapy or lymphodepletion. Of these 32 patients, 20 received cilta-cel as a subsequent therapy.



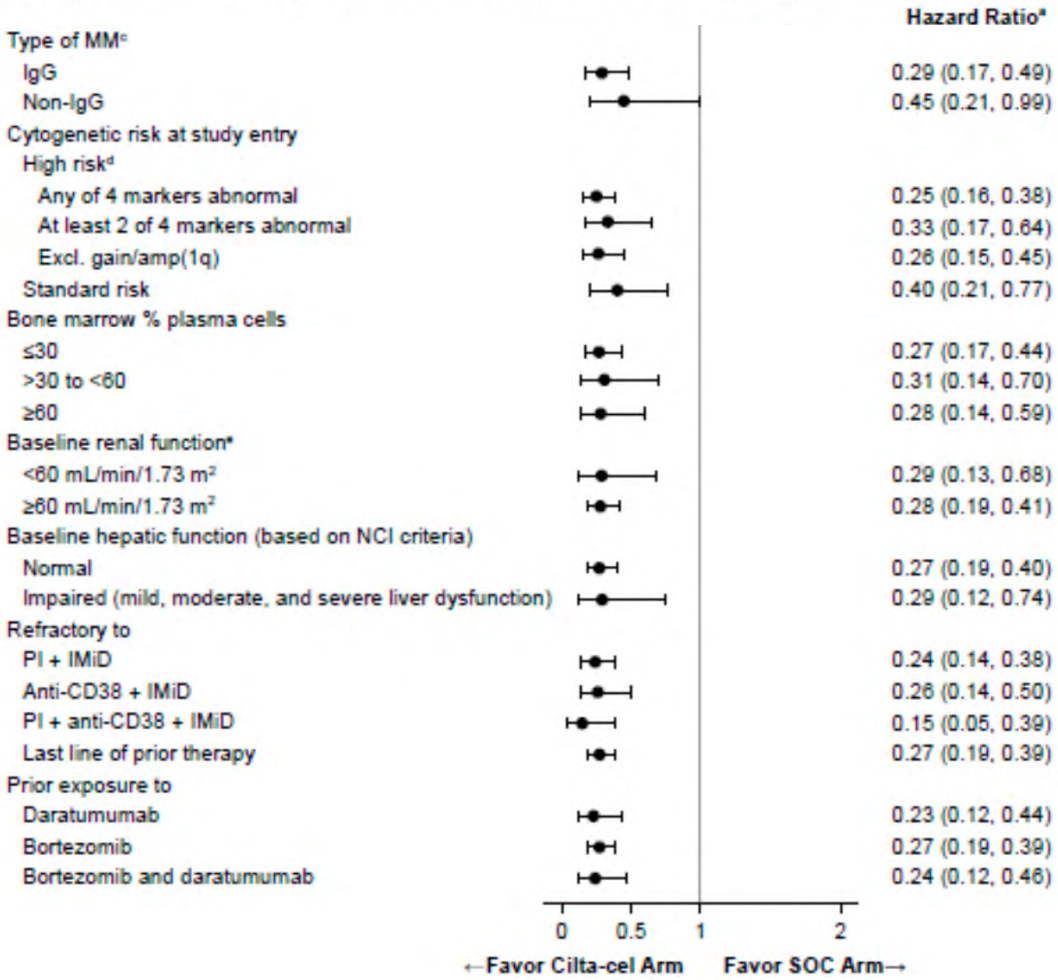

**No. at Risk**

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Cilta-cel group | 208 | 177 | 172 | 166 | 146 | 94 | 45 | 22 | 9 | 1 | 0 |
| Standard-care group | 211 | 176 | 133 | 116 | 88 | 46 | 20 | 4 | 1 | 0 | 0 |

**Supplemental Figure 1.** Forest plot of subgroup analysis on progression-free survival



**Supplemental Figure 1.** Forest plot of subgroup analysis on progression-free survival



# Carvykti

- PI+IMID exposed and refractory to lenalidomid
- z.B. Dara-VTd + Len-Erhaltung oder VRD
- Szenario 1: nicht CD38 AK-refraktär:
- CD38+Kd, mPFS 35.7 Mo (IKEMA), 28.6 Mo (CANDOR)
- Szenario 2: CD38 AK refraktär:
- Brigding: z.B. Kd oder PVd
- Szenario 3: CD38 AK refraktär, PI non-exposed???
- z.B. nach DRd: Kd oder PVd als bridging vor Carvykti?
- Szenario 4: PI,IMID und CD38 AK vorbehandelt aber nicht Len-refraktär wegen Absetzen bei Unverträglichkeit: Medizinisch wie Len-refraktär einstufen und damit Carvykti in label?

# Indikation zur BCMA Therapie 2024

- 2 Vortherapien inkl. PI, IMID, CD38: Abecma und Carvykti
- 1 Vortherapie inkl. PI, IMID, CD38: Carvykti
- 1 Vortherapie inkl. PI, IMID: Carvykti oder CD38 AK + Kd?
- 1 Vortherapie inkl. IMID, CD38: PVd (oder Carvykti?)
- 1 Vortherapie inkl. PI, IMID, CD38, aber Len-Abbruch wegen Tox: Carvykti?

- Bi-spezifische Antikörper erst nach CART oder bei fehlender CART Eignung
- Zulassung erst nach 3 Vortherapien