Nowe doniesienia w szpiczaku plazmocytowym po spotkaniu ASH 2018

ARTUR JURCZYSZYN MD, PhD Assoc. Prof.

Jagiellonian University Medical College Department of Haematology

- Badanie MAIA – late breaking abstract
- Badanie Ird_DARA
- Badanie Rd-R vs Rd u Chorych z de novo MM
- Badanie FORTE – KRd – badanie włoskie
- Badania z SELINEXOREM
- Wykorzystanie komórek CAR T oraz BiTes
- Amyloidoza – wykorzystanie BENDAMUSTYNY
- Badania własne z Krakowa – 3 PLAKATY

2018 FDA Approvals for Hematology Indications*

● New Molecular Entity
▲ Biosimilar

Non-Malignant / Hematology Support

Malignant

Jan

Feb

Mar

Apr

May

Jun

Jul

Aug

Sep

Oct

Nov

Dec

● **coagulation factor Xa (recomb), inactivated-zhzo** (reversal of anticoag due to life-threatening or uncontrolled bleeding with apixaban or rivaroxaban)

denosumab (prevention of skeletal events in MM)

● **fostamatinib** (chronic ITP, prev. treated)

● **avatrombopag** (thrombocytopenia with chronic liver disease, peri-procedural)

▲ **epoetin alfa-epbx** (biosimilar to Epogen/ Procrit)

▲ **pegfilgrastim-jmdb** (biosimilar to Neulasta)

methoxy PEG-epoetin beta (anemia due to pediatric CKD)

▲ **filgrastim-aafi** (biosimilar to Neupogen)

● **lusutrombopag** (thrombocytopenia with chronic liver disease, peri-procedural)

● **antihemophilic factor (recomb), PEGylated-aucl** (hemophilia A, previously treated)

emicizumab-kxwh (prophylaxis in hemophilia A without inhibitors)

▲ **pegfilgrastim-cbqv** (biosimilar to Neulasta)

eltrombopag (severe aplastic anemia, prev. untreated, in comb. with IST)

● **emapalumab-lzsg** (primary HLH, refractory or recurrent)

arsenic trioxide (newly diagnosed low-risk APL, in comb. with ATRA)

brentuximab vedotin (newly diagnosed St. 3 or 4 cHL, in comb. with chemotherapy)

nilotinib (pediatric CML)

blinatumomab (pre-B ALL in CR1 or CR2 with MRD≥0.1%)

tisagenlecleucel (R/R large B-cell lymphoma)

daratumumab (newly diagnosed MM, transplant-ineligible, in comb. with VMP)

venetoclax (CLL/SLL, after at least 1 prior therapy)

pembrolizumab (R/R primary mediastinal large B-cell lymphoma)

● **ivosidenib** (R/R AML with IDH1 mutation)

● **mogamulizumab-kpkc** (R/R mycosis fungoides or Sezary Syndrome)

● **moxetumumab pasudotox-tdfk** (R/R hairy cell leukemia, after ≥ 2 prior therapies)

● **duvelisib** (R/R CLL/SLL, after ≥ 2 prior ther.) (R/R FL after ≥ 2 prior ther.)

elotuzumab (R/R MM, in comb. with PomDex)

brentuximab vedotin (newly diagnosed PTCL, in comb. with chemo)

venetoclax (newly diag. AML†, in comb.)

● **glasdegib** (newly diag. AML†, in comb.)

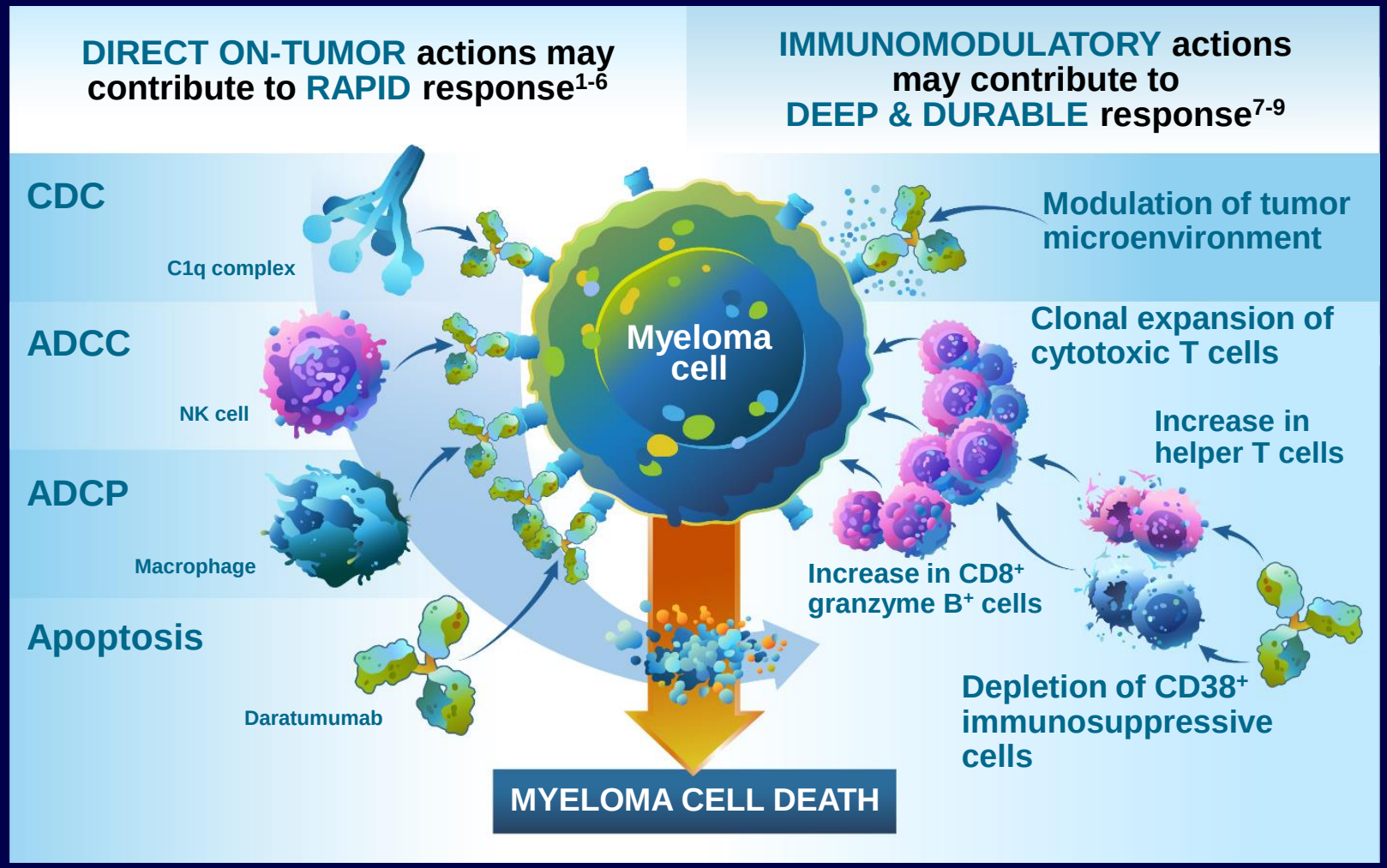
● **gilterinib** (FLT-3 mut AML, prev. treated)

▲ **rituximab-abbs** (biosimilar to Rituxan, FL and low-grade lymphoma)

**Refer to US Prescribing Information for details.*

†age ≥ 75y, or with comorbidities that preclude intensive chemo

Daratumumab



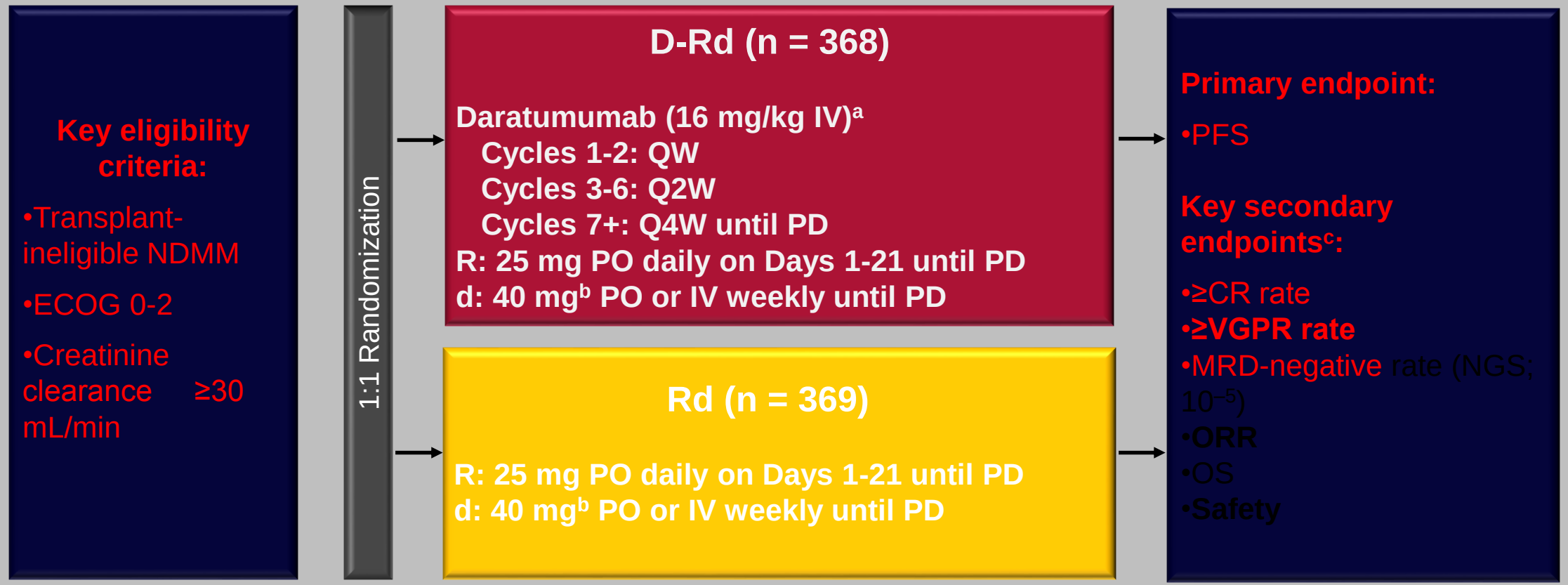
- Daratumumab
  - Human IgGκ monoclonal antibody targeting CD38 with direct on-tumor and immunomodulatory mechanisms of action
- Approved
  - As **monotherapy** and in **combination** with standard-of-care regimens in RRMM in many countries
  - In **combination** with bortezomib, melphalan, and prednisone in **transplant-ineligible NDMM** in many countries
- Efficacy
  - Daratumumab-based combinations reduce risk of progression or death and induce rapid, deep, and durable responses across all lines of therapy[10-12]

CDC, complement-dependent cytotoxicity; ADCC, antibody-dependent cellular cytotoxicity; NK, natural killer; ADCP, antibody-dependent cellular phagocytosis; RRMM, relapsed or refractory multiple myeloma; NDMM, newly diagnosed multiple myeloma.

1. DARZALEX US PI; 2018. 2. Liszewski MK, et al. *Adv Immunol*. 1996;61:201-283. 3. Debets JM, et al. *J Immunol*. 1988;141(4):1197-1201. 4. Overdijk MB, et al. *mABs*. 2015;7(2):311-321. 5. Lokhorst HM, et al. *N Engl J Med*. 2015;373(13):1207-1219. 6. Plesner T, et al. *Blood*. 2012;120:73. 7. Krejcik J, et al. *Blood*. 2016;128(3):384-394. 8. Adams H, et al. Poster presented at: ASH; December 3-6, 2016; San Diego, CA. 9. Chiu C, et al. Poster presented at: ASH; December 3-6, 2016; San Diego, CA. 10. Palumbo A, et al. *N Engl J Med*. 2016;375(8):754-766. 11. Dimopoulos MA, et al. *N Engl J Med*. 2016;375(14):1319-1331. 12. Mateos MV, et al. *N Engl J Med*. 2018;378:518-528.

MAIA Study Design

- Phase 3 study of D-Rd vs Rd in transplant-ineligible NDMM (N = 737)



Stratification factors
- ISS (I vs II vs III)
- Region (NA vs other)
- Age (<75 vs ≥75 years)

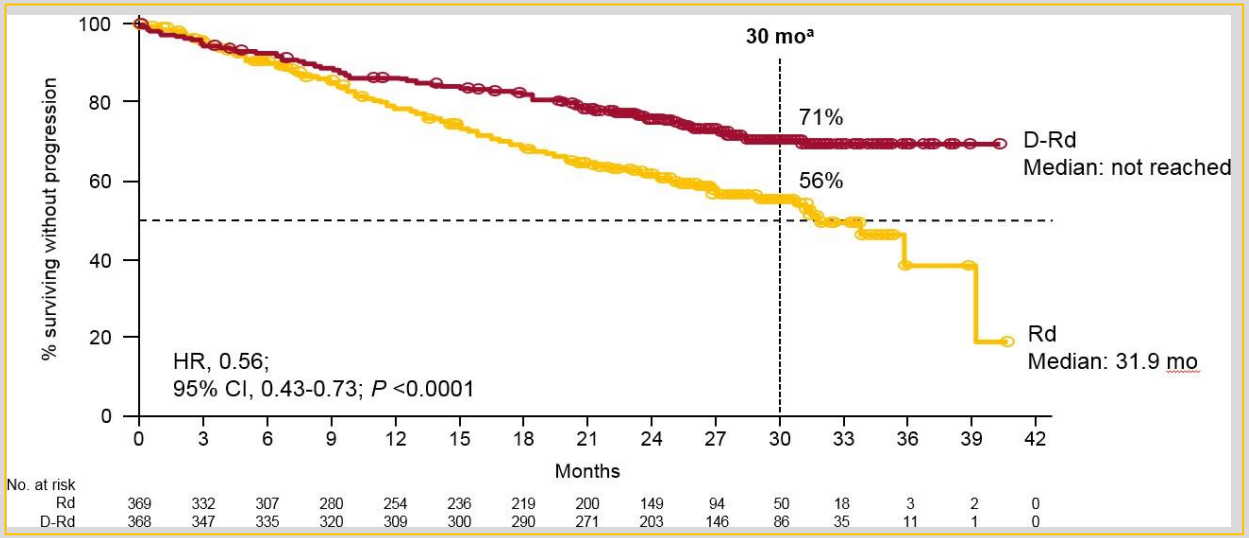
Cycle: 28 days

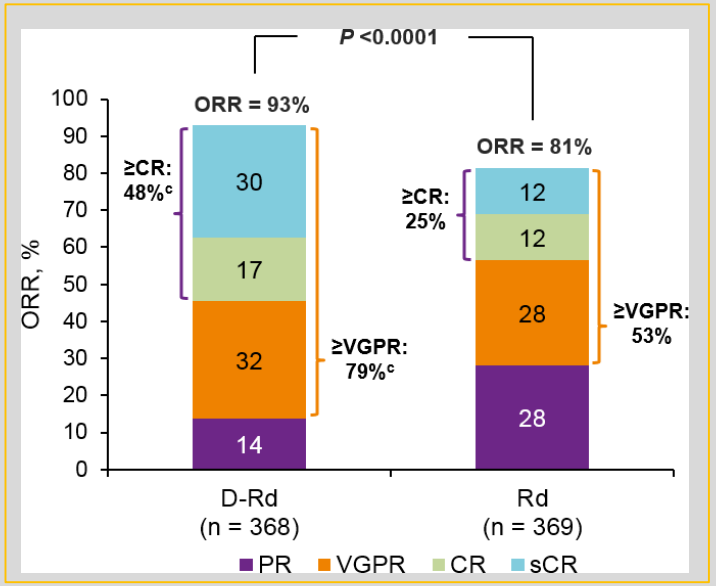
[a]On days when daratumumab was administered, dexamethasone was administered to patients in the D-Rd arm and served as the treatment dose of steroid for that day, as well as the required pre-infusion medication.
[b]For patients older than 75 years of age or with BMI <18.5, dexamethasone was administered at a dose of 20 mg weekly.
[c]Efficacy endpoints were sequentially tested in the order shown.

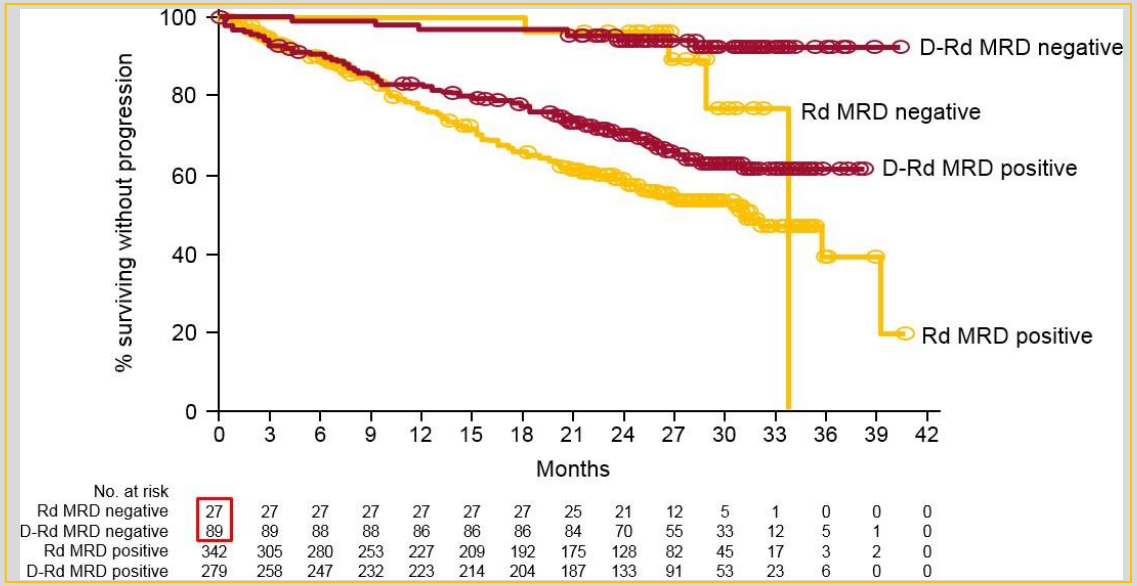
ECOG, Eastern Cooperative Oncology Group; ISS, International Staging System; NA, North America; IV, intravenously; QW, once weekly;
Q2W, every 2 weeks; Q4W, every 4 weeks; PD, progressive disease; PO, orally; CR, complete response; VGPR, very good partial response; MRD, minimal residual disease; NGS, next-generation sequencing; ORR, overall response rate; OS, overall survival;

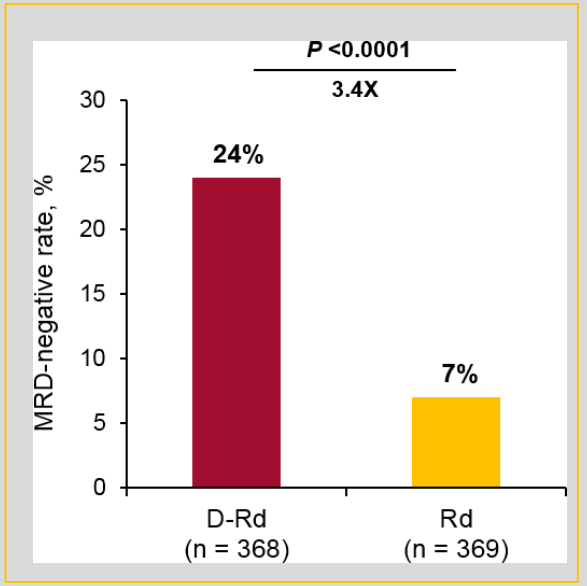
EFFICACY: ORR AND PFS

Median follow-up: 28 months (range: 0.0-41.4)









Facon T, et al. ASH 2018 [abstract LBA-2].

Phase 2 trial of Ixazomib, Lenalidomide, Dexamethasone and Daratumumab in Patients with Newly Diagnosed Multiple Myeloma

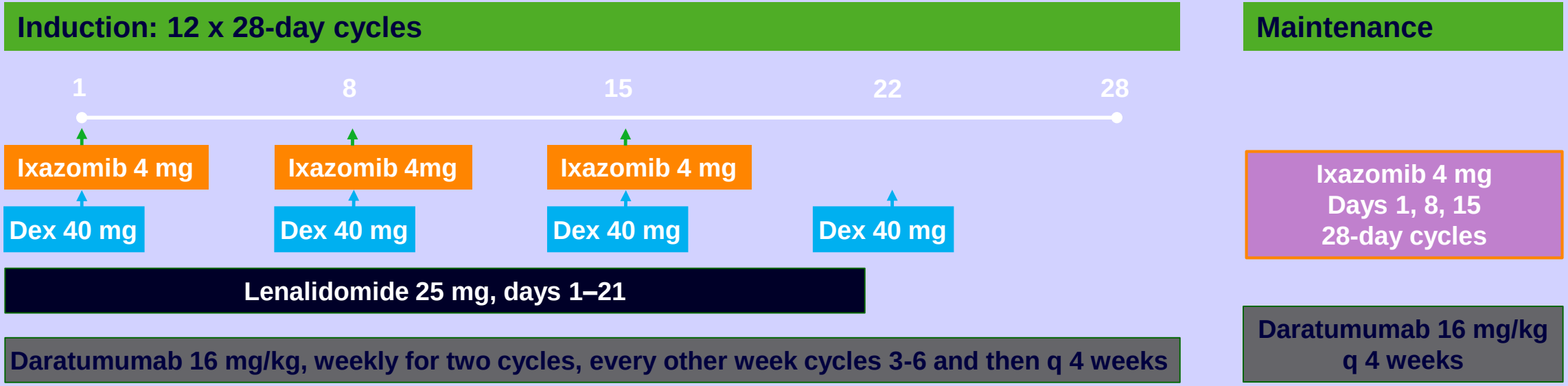
Shaji Kumar, Prashant Kapoor, Betsy LaPlant, Eli Muchtar, Eric Wolfe, Francis Buadi, Wilson Gonsalves, Angela Emanuel, David Dingli, Ronald Go, Rahma Warsame, Taxiarchis Kourelis, John Lust, Martha Lacy, Angela Dispenzieri, Suzanne Hayman, Lisa Hwa, Amie Fonder, Miriam Hobbs, Nelson Leung, S. Vincent Rajkumar, Morie Gertz

Scottsdale, Arizona

Rochester, Minnesota

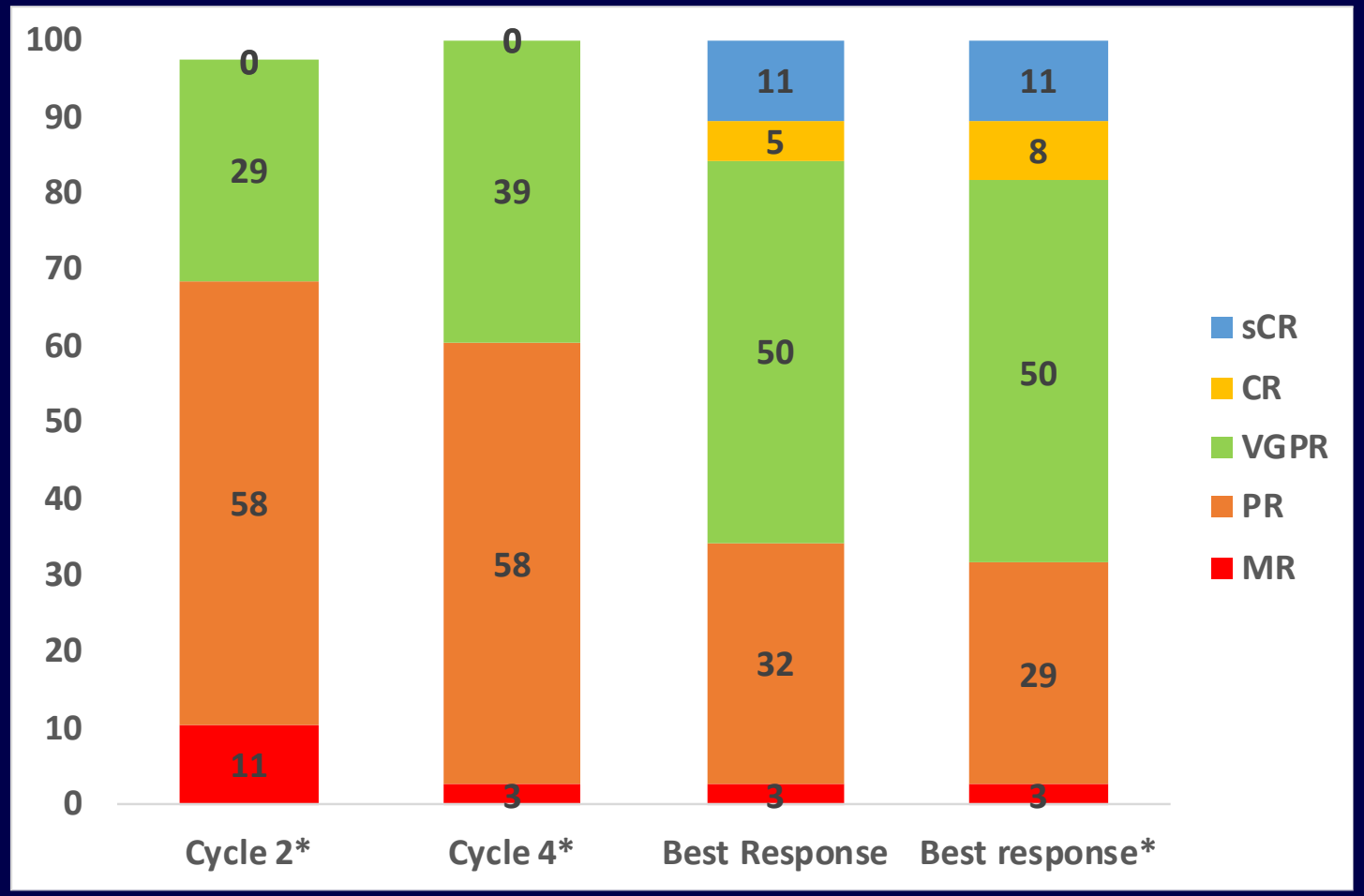
Jacksonville, Florida

Schemat badania



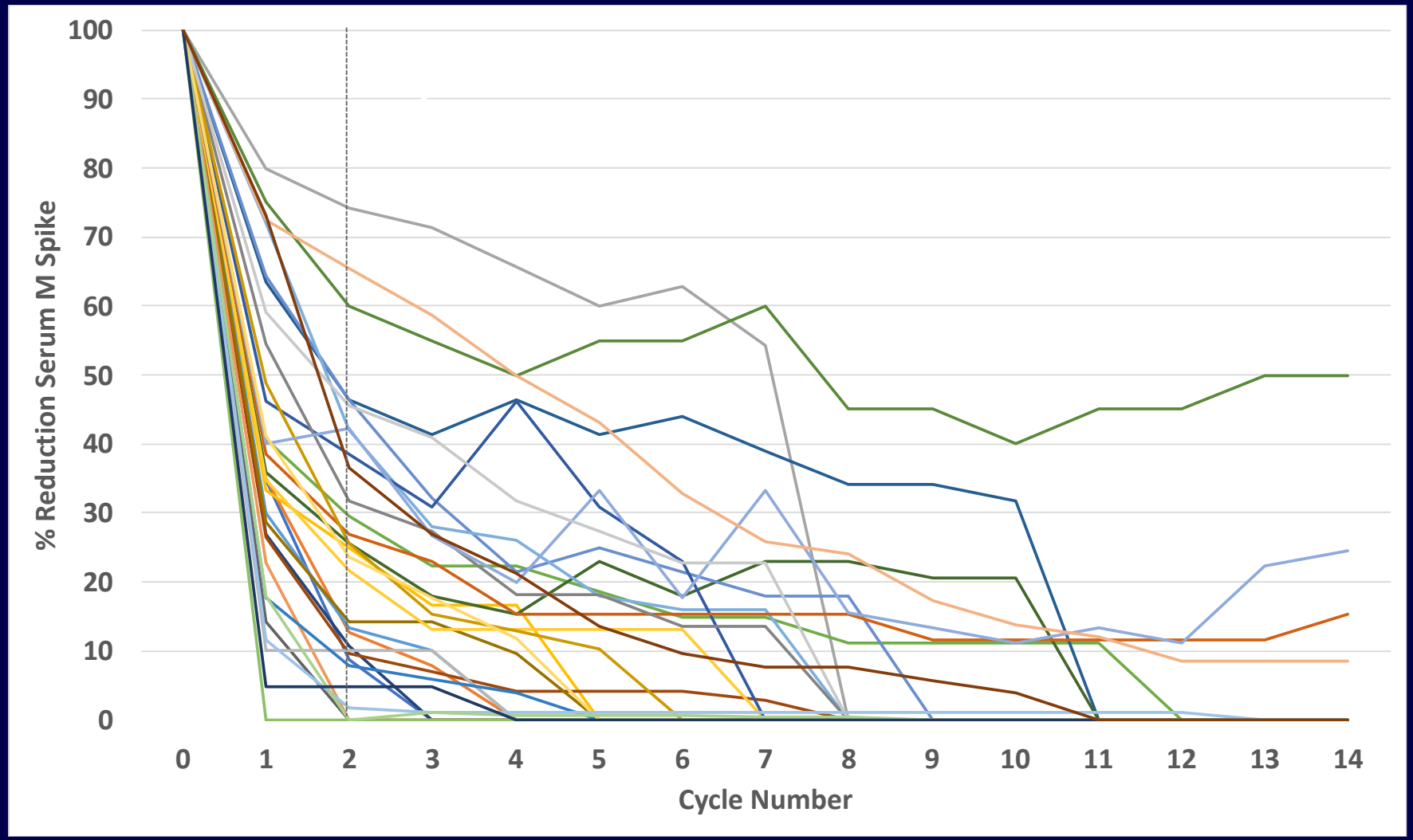
- Standard infectious disease, bone, and thrombosis prophylaxis
- Treatment till progression or unacceptable toxicity or to a maximum of 3 years
- Stem cells could be collected after 4 cycles if SCT eligible

ODPOWIEDZ na leczenie



** Including unconfirmed responses*

Kinetics of response



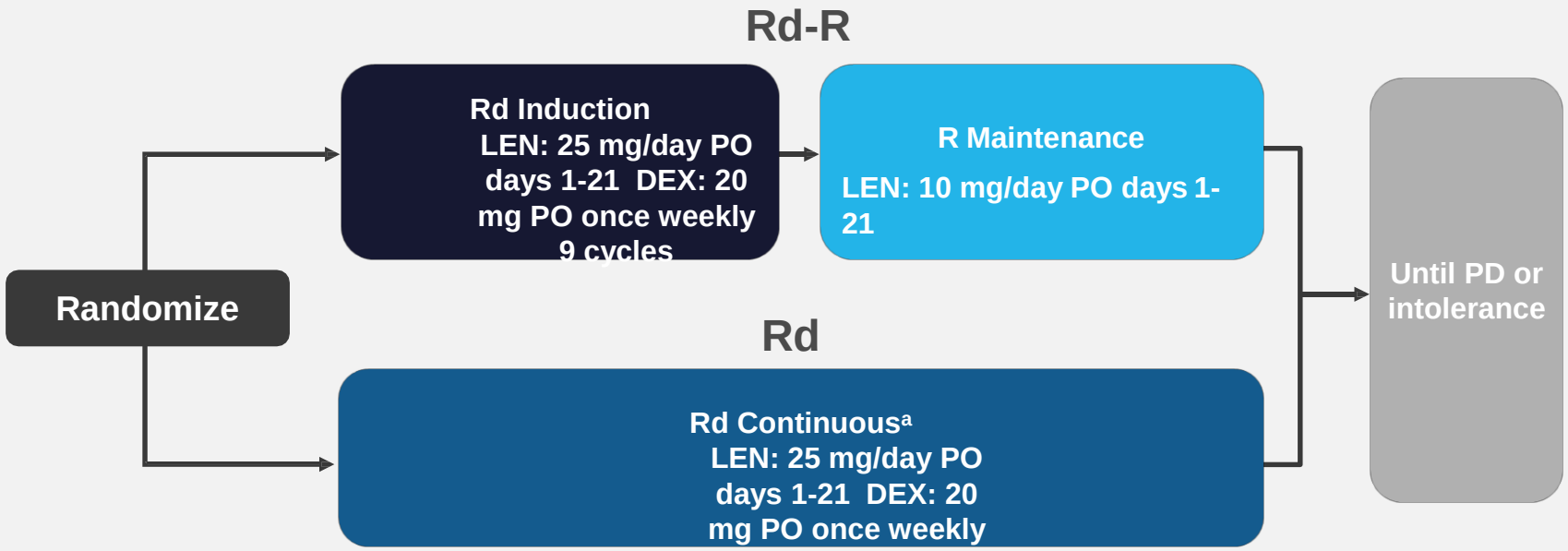
ABSTRACT 305

Efficacy and Feasibility of Dose/Schedule-Adjusted Rd-R Vs Continuous Rd in Elderly and Intermediate-Fit Newly Diagnosed Multiple Myeloma (NDMM) Patients: RV-MM-PI-0752 Phase 3 Randomized Study

Alessandra Larocca,[1] Marco Salvini,[1] Lorenzo De Paoli,[1] Nicola Cascavilla,[1] Giulia Benevolo,[1] Monica Galli,[1] Vittorio Montefusco,[1] Tommaso Caravita di Toritto,[1] Anna Baraldi,[1] Stefano Spada,[1] Nicola Giuliani,[1] Chiara Pautasso,[1] Stefano Pulini,[1] Sonia Ronconi,[1] Norbert Pescosta,[1] Anna Marina Liberati,[1] Francesca Patriarca,[1] Claudia Cellini,[1] Patrizia Tosi,[1] Massimo Offidani,[1] Michele Cavo,[1] Antonio Palumbo,[2] Mario Boccadoro,[1] Sara Bringhen[1]
on behalf of co-investigators

[1]GIMEMA/European Myeloma Network, Italy; [2]Univesity of Torino - Currently Takeda Pharmaceuticals Co.

STUDY DESIGN[1]



- N=199 intermediate-fit patients
- Primary endpoint:
  - EFS
    - Hematologic grade 4 AEs
    - Non-hematologic grade 3/4 AEs, including SPMs
    - LEN therapy discontinuation
    - PD
    - Death due to any cause
- Secondary endpoints:
  - PFS
  - OS
  - Response rate
  - Incidence of dose reduction and discontinuation

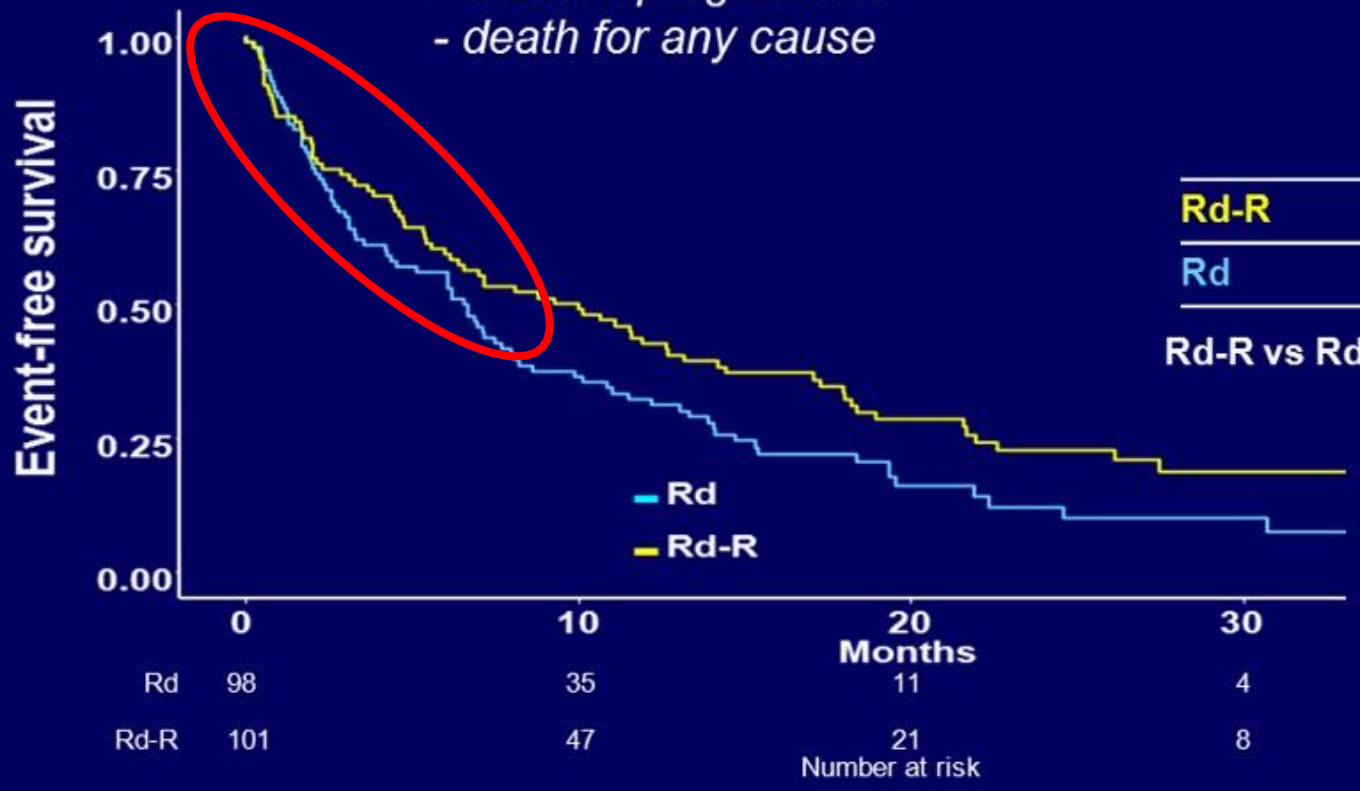
[a] Dose and schedule adopted in the FIRST trial in patients > 75 years[2].

1. Larocca A, et al. ASH 2018 [abstract 1305]. 2. Hulin C, et al. *J Clin Oncol.* 2016;34:3609-3617

EVENT FREE SURVIVAL

Median follow-up 25 months

Definition of the event:- hematologic grade 4 AEs*
- non-hematologic grade 3-4 AEs including SPM
- discontinuation of lenalidomide therapy
- disease progression
- death for any cause



	Median EFS
Rd-R	9.3 months
Rd	6.6 months

Rd-R vs Rd: HR 0.72; CI 0.52-0.99; p=0.044

* Related to study drugs

AUTHORS CONCLUSIONS

	Rd-R	Rd	Rd FIRST >75 Years
Age > 75 years	48%	57%	35%
EFS *(toxicity, discontinuation, PD, death)*	9.3 months	6.6 months	NA
At least 1 non-hematologic grade ≥3 tox	**31%**	**39%**	**NA**
R discontinuation	**19%**	**23%**	**26%**
R dose reduction	**33%**	**43%**	**44%**
R dose reduction after induction	**14%**	**21%**	**NA**
R Median Relative Dose Intensity	**100%**	**90%**	**NA**
20-month PFS	43%	42%	≈50%
20-month OS	84%	79%	≈80%

Comparable Efficacy Rd = Rd-R

Improved Tolerance/Feasibility Rd-R > Rd

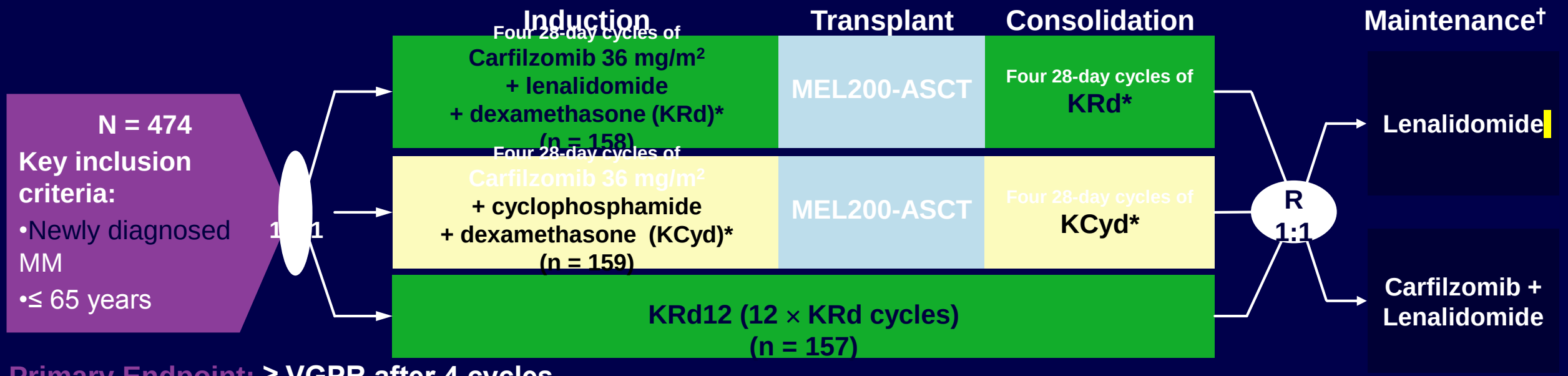
Hulin C, et al JCO 2016. Benboubker L et al N Engl J Med 2014.

Carfilzomib-Lenalidomide-Dexamethasone (KRd) induction-Autologous Transplant (ASCT)-KRd consolidation vs KRd 12 cycles vs Carfilzomib-Cyclophosphamide-Dexamethasone (KCyd) induction-ASCT-KCyd consolidation: Analysis of the Randomized FORTE Trial in newly diagnosed Multiple Myeloma (NDMM)

Gay F, et al. Oral Abstract Session, ASH Annual Meeting; December 1–4, 2018; San Diego, CA, USA. Abstract 121.

FORTE Trial: Randomized Trial of KRd ± ASCT vs KCyd + ASCT in patients with NDMM

- Objective: To evaluate the efficacy and safety of KRd induction-ASCT-KRd consolidation (KRd-ASCT-KRd) vs 12 cycles of KRd (KRd12) vs KCyd induction-ASCT-KCyd consolidation (KCyd-ASCT-KCyd)
- Patients were stratified based on ISS and age



Primary Endpoint: ≥ VGPR after 4 cycles
Secondary Endpoint: Pre-maintenance sCR, MRD negativity rate in ITT‡

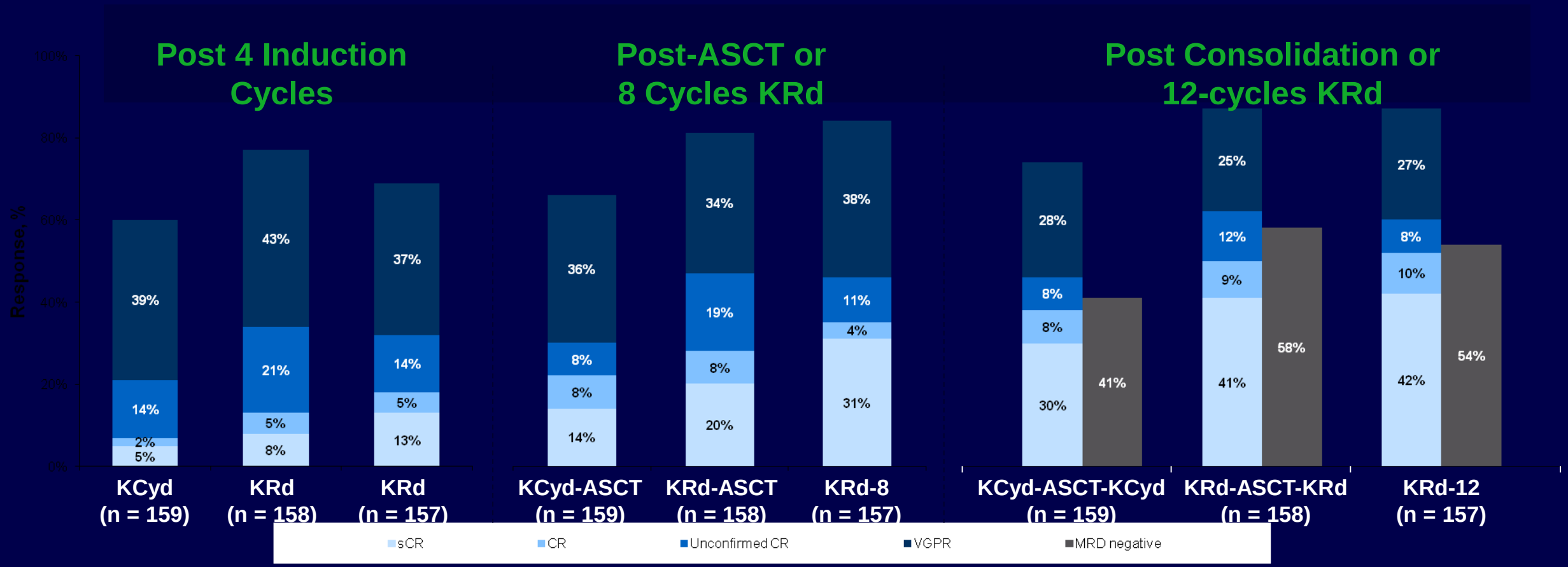
*Four 28-day cycles, carfilzomib taken twice weekly, on days 1,2,8,9,15,16. †Median follow-up was 20 months; data cutoff was May 30, 2018. ‡MRD evaluation was performed on a eight-color second-generation flow cytometer (Sensitivity 10^{-5}) on patients achieving ≥ VGPR

1. Gay F, et al. Presented at: ASH Annual Meeting; December 1–4, 2018; San Diego, CA, USA. Abstract 121. 2. ClinicalTrials.gov. NCT02203643. Available at: https://www.clinicaltrials.gov/ct2/show/NCT02203643. Accessed November 8, 2018

Data, comments, and/or conclusions on this slide are based on the congress abstract and represent authors' findings and views that are independent of Amgen

FORTE Trial: Randomized Trial of KRd ± ASCT vs KCyd + ASCT in patients with NDMM

Response Rates



The depth of response was significantly higher in KRd arms vs KCyd; similar rates of MRD negativity were reported in the KRd arms

ASCT, autologous stem cell transplant; CR, complete response; KCyd, carfilzomib + cyclophosphamide + dexamethasone; KRd, carfilzomib + lenalidomide + dexamethasone; KRd12, 12 cycles of KRd; MRD, minimal residual disease; sCR, stringent complete response; VGPR, very good partial response.

Gay F, et al. Presented at: ASH Annual Meeting; December 1–4, 2018; San Diego, CA, USA. Abstract 121.

Data, comments, and/or conclusions on this slide are based on the congress abstract and represent authors' findings and views that are independent of Amgen

FORTE Trial: Randomized Trial of KRd ± ASCT vs KCyd + ASCT in patients with NDMM

Adverse Events

Most frequent grade 3 or 4 AEs*, %	KCyd-ASCT-KCyd	KRd-ASCT-KRd	KRd12
Neutropenia	16	20	10
Thrombocytopenia	13	15	8
Infections	13	14	12
Grade 3 or 4 dermatologic AEs	1	5	12
Increase in liver enzymes	1	9	10
Hypertension	3	3	8
Grade 3 or 4 cardiac AEs	4	3	2
Thrombosis	2	1	2
Discontinuation due to AEs during treatment	7	6	8

- Median follow-up: 20 months

Rates of discontinuation due to AEs during treatment were similar between the three arms and treatments were well tolerated

Data, comments, and/or conclusions on this slide are based on the congress abstract and represent authors' findings and views that are independent of Amgen

ABSTRACT 598

Results of the Pivotal STORM Study (Part 2) in Penta-Refractory Multiple Myeloma (MM): Deep and Durable Responses With Oral Selinexor Plus Low Dose Dexamethasone in Patients with Penta Exposed and Triple Class-Refractory MM

Ajai Chari, Dan T. Vogl, Meletios A. Dimopoulos, Ajay K. Nooka, Carol Ann Huff, Philippe Moreau, Craig E. Cole, Joshua Richter, David Dingli, Ravi Vij, Sascha A. Tuchman, Marc S. Raab, Katja Weisel, Michel Delforge, David Kaminetzky, Robert Frank Cornell, A. Keith Stewart, James Hoffman, Kelly N. Godby, Terri L. Parker, Moshe Levy, Martin Schreder, Nathalie Meuleman, Laurent Frenzel, Mohamad Mohty, Choquet Sylvain, Andrew J. Yee, Maria Gavriatopoulou, Luciano J. Costa, Jatin J. Shah, Carla Picklesimer, Jean-Richard Saint-Martin, Lingling Li, Michael G. Kauffman, Sharon Shacham, Paul Richardson, Sundar Jagannath

Oral presentation at the 60th Annual Meeting of the American Society of Hematology December 1–4, 2018

Monday, December 3, 2018 at 07:45 hours

Sd IN PENTA-REFRACTORY MM PATIENTS
STUDY DESIGN, PATIENT CHARACTERISTICS, AND RESULTS

Phase 2 STORM (Part 2)

Penta-refractory MM (N = 122)

- Previously treated with BORT, CFZ, LEN, POM, DARA, an alkylator, and glucocorticoids
- Refractory to ≥ 1 PI, ≥ 1 IMiD, DARA, glucocorticoid, and last

→ **Sd**
SEL: 80 mg twice weekly
DEX: 20 mg twice weekly

Patient Characteristics	N = 122
Median age (range), years	65 (40–86)
Median time from diagnosis (range), years	6.6 (1.1–23.4)
High risk cytogenetics, n (%)	65 (53)
Median prior treatment regimens (range), n	7 (3–18)
CFZ, POM, DARA refractory, n	117 (96)
(%) Prior DARA-based therapy n	86 (70)
(%) Prior stem cell transplant, n	102 (84)
(%) Prior CAR T therapy, n (%)	2 (2)

Efficacy Outcomes	N = 122
ORR, %	26.2
Stringent CR	1.6
VGPR	4.9
PR	19.7
CBR (≥ MR), %	39.3
≥ SD, %	78.7
Median response duration, months	4.4
Median OS, months	8.6
Median PFS, months	3.7

- Primary endpoint: ORR
- Secondary endpoints: response duration, CBR, OS, PFS, safety
- 2 patients who progressed on CAR T therapy achieved PR
- Most common (> 10%) grade 3 and 4 treatment-related AEs, respectively, included: thrombocytopenia (22.8% and 30.9%), anaemia (28.5% and 0.8%), neutropenia (15.4% and 3.3%), fatigue (18.7% and 0%), hyponatraemia (16.3% and 0%), and leucopenia (13.0% and 0%)
  - AEs were typically reversible and manageable with dose modification and supportive care

AUTHORS' CONCLUSIONS:

- SEL is the first oral agent with activity in very heavily pretreated, penta-exposed, triple class-refractory MM patients

AE, adverse event; BORT, bortezomib; CAR T, chimeric antigen receptor T-cell; CBR, clinical benefit rate; CFZ, carfilzomib; CR, complete response; DARA, daratumumab; DEX, dexamethasone; IMiD, immunomodulatory drug; LEN, lenalidomide; MR, minimal response; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PI, proteasome inhibitor; POM, pomalidomide; PR, partial response; Sd, selinexor + low-dose dexamethasone; SEL, selinexor; SD, stable disease.

Chari et al. ASH 2018: Abstract 598. Oral presentation

ABSTRACT 599

Selinexor, Daratumumab, and Dexamethasone (SDd) in Patients with MM Previously Exposed to PIs and IMiDs: Results of Phase 1b Study of SDd

Selinexor Plus Pomalidomide and Low Dose Dexamethasone (SPd) in Patients with Relapsed or Refractory Multiple Myeloma

Cristina J. Gasparetto, Suzanne Lentzsch, Gary J. Schiller, William Bensinger, Nizar Bahlis, Heather J. Sutherland, Darrell J. White, Michael Sebag, Rami Kotb, Christopher P. Venner, Richard Leblanc, Christine I. Chen, Aldo Del Col, Jatin J. Shah, Jacqueline Jeha, Jean-Richard Saint-Martin, Michael G. Kauffman, Sharon Shacham, Joel G. Turner, Daniel M. Sullivan, Brea Lipe

Christine I. Chen, Heather J. Sutherland, Rami Kotb, Michael Sebag, Darrell J. White, William Bensinger, Cristina J. Gasparetto, Richard Leblanc, Christopher P. Venner, Suzanne Lentzsch, Gary J. Schiller, Brea Lipe, Aldo Del Col, Jatin J. Shah, Jacqueline Jeha, Jean-Richard Saint-Martin, Michael G. Kauffman, Sharon Shacham, Nizar Bahlis

SDd TREATMENT IN PATIENTS WITH PI / IMiD-REFRACTORY MM STUDY DESIGN, SAFETY, AND EFFICACY

- Phase 1b/2 study to determine the MTD and RP2D of SDd
  3 + 3 Dose Escalation

N = 28
•≥ 3 prior lines of MM therapy including a PI and an IMiD; or
•Patients with MM refractory to a PI and an IMiD

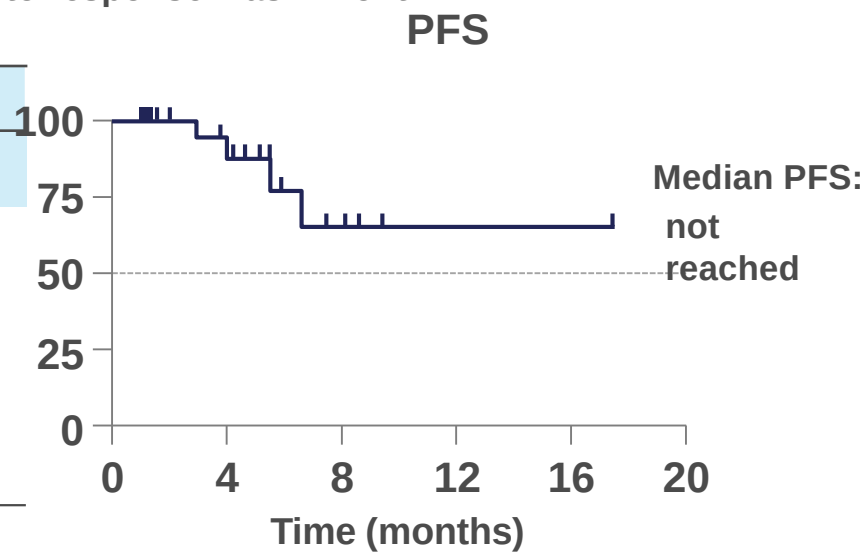
Dose Level 0 (n = 3)
SEL: 60 mg biw p.o.
DARA: 16 mg/kg i.v. qw
DEX: 20 mg p.o. qw

Dose Level −1 (n = 25)
SEL: 100 mg qw p.o.
DARA: 16 mg/kg i.v. qw
DEX: 40 mg p.o. qw

- Baseline characteristics:
  - median age of 68 years (44–77),
  - median of 3 (2–10) prior regimens
  - 61% PI-ref, 64% IMiD-ref
  - Prior-ASCT 79%
  - Median time since diagnosis 5.9yr
- The RP2D was dose level −1: SEL 100 mg, DARA 16 mg/kg, and DEX 40 mg qw

Most Common (> 10 %) Grade 3 or 4 AEs, n (%)	At RP2D (n = 25)	
	Grade 3	Grade 4
Thrombocytopenia	7 (28)	4 (16)
Leukopenia	7 (28)	0
Anaemia	7 (28)	0
Neutropenia	6 (24)	0
Lymphopenia	3 (12)	1 (4)
Hyponatraemia	3 (12)	0
Fatigue	3 (12)	0

- ORR (N = 26) was 73% (27% VGPR, 46% PR) and CBR was 81% (8% MR)
  - Among 24 DARA-naive patients, the ORR was 79% (29% VGPR, 50% PR) and CBR was 88% (8% MR)
  - SD occurred in 4 (15%) patients and 1 (4%) patient progressed
- Median treatment duration was 7.3 months in patients with ≥ PR
- Median time to response was 1 month



AUTHORS' CONCLUSIONS:

- SDd appears to be highly active, produces deep and durable responses with patients with RRMM, and warrants further

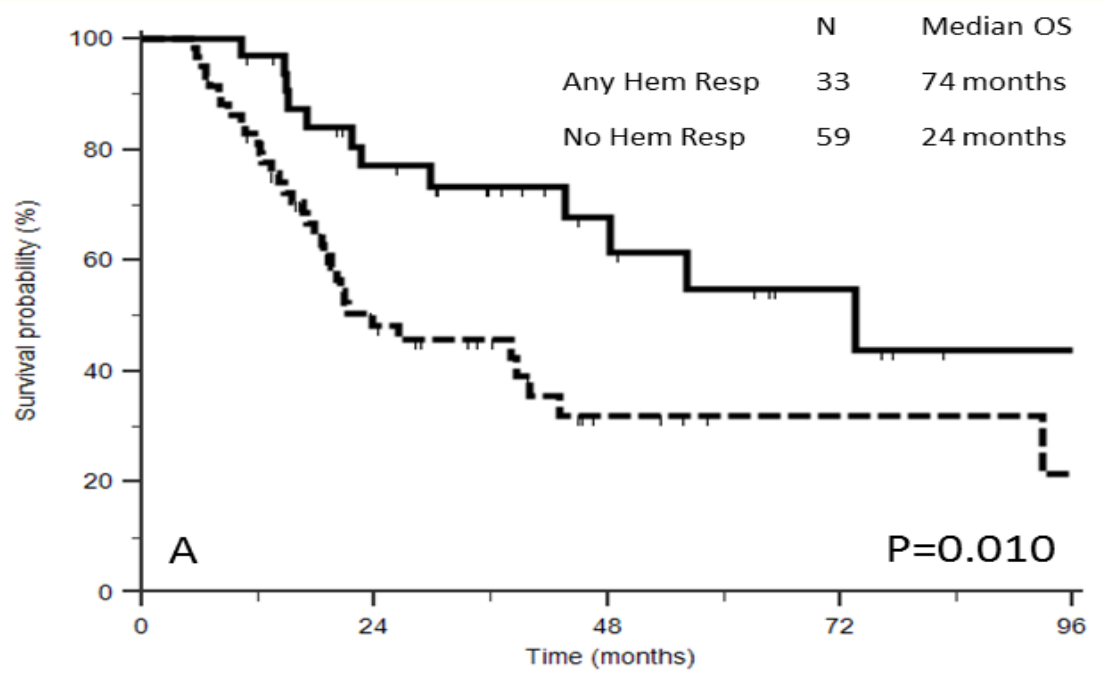
AE, adverse event; biw, twice weekly; CBR, clinical benefit rate; DARA, daratumumab; DEX, dexamethasone; DLT, dose-limiting toxicity; IMiD, immunomodulatory drug; MTD, maximum tolerated dose; MR, minimal response; ORR, overall response rate; PFS, progression-free survival; PI, protease inhibitor; p.o., orally; PR, partial response; qw, once weekly; RP2D, recommended phase 2 dose; SD, stable disease; SEL, selinexor; VGPR, very good partial response.

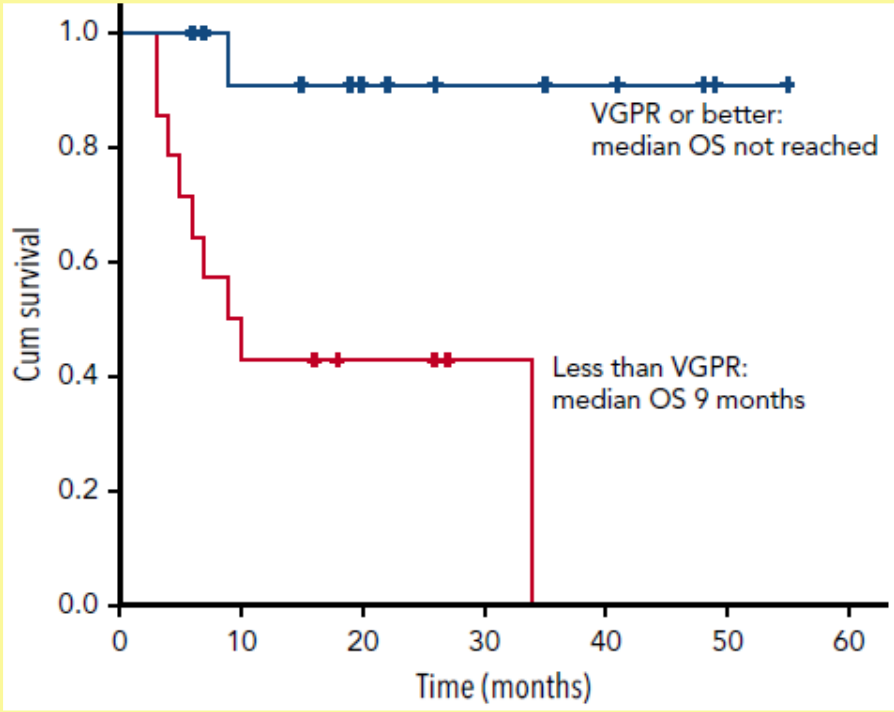
Gasparetto et al. ASH 2018: Abstract 599. Oral presentation

AMYLOIDOSIS - Newer (and older) chemotherapy approaches - Bendamustine

Hematologic response

- **35% (CR 2%, VGPR 8%)**
- **55-59% in patients with IgM-AL (CR 8-11%, VGPR 25-37%)**

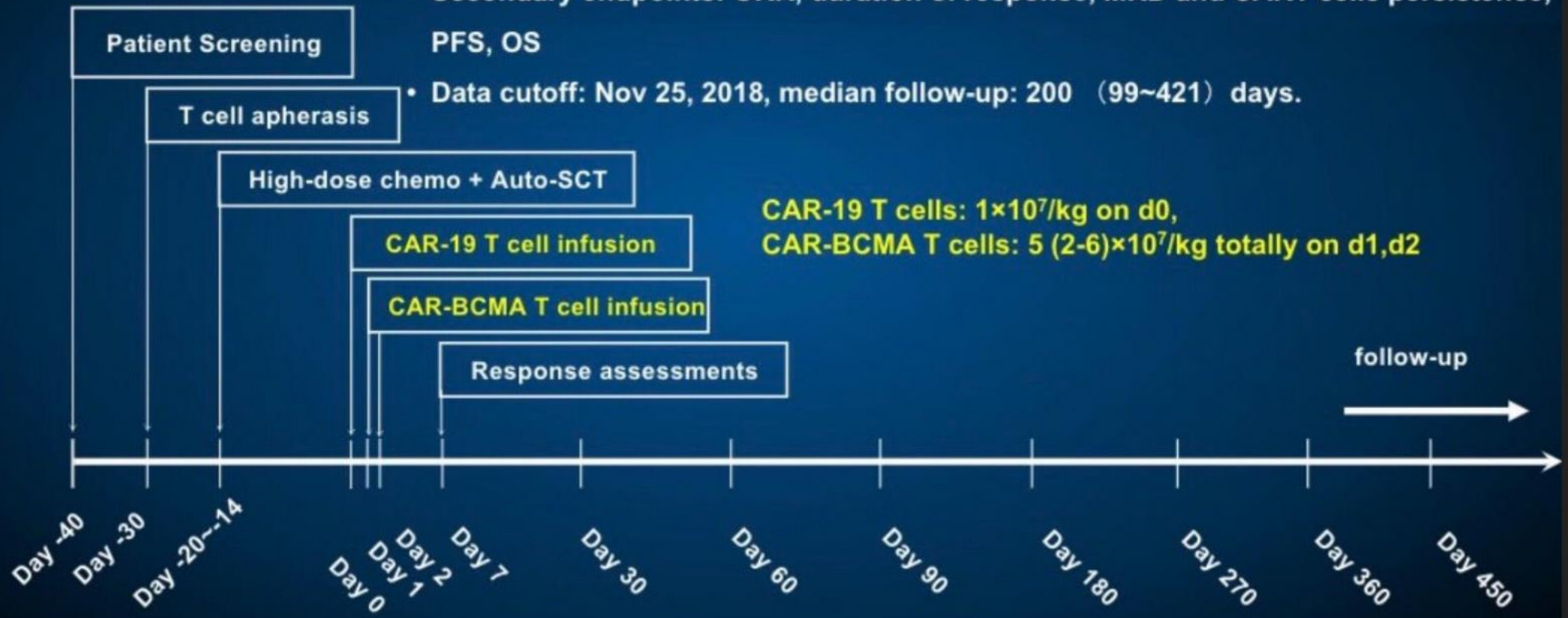




1. *Milani, et al. Blood 2018*
2. *Manwani, et al. Blood 2018*

SZ-CART-MM 02 Study: CD19 and BCMA CART Cells for High Risk MM Followed With Auto-HSCT (NCT 03455972)

- Primary endpoints: safety, tolerability
- Secondary endpoints: ORR, duration of response, MRD and CART cells persistence, PFS, OS
- Data cutoff: Nov 25, 2018, median follow-up: 200 （99~421） days.



CAR-19 T cells: 1×10^7/kg on d0,
CAR-BCMA T cells: 5 (2-6)$\times10^7$/kg totally on d1,d2

Xiaolan Shi et al. ASH 2018; Oral presentation, Abstact 1009.

The Prognostic Impact of t(14;16) in Multiple Myeloma: A Multicenter Retrospective Study of 213 Patients. Is it time to revise the revised ISS?

Artur Jurczyszyn (1), Sarah Goldman-Mazur (1), Jorge J. Castillo (2), Anna Waszczuk-Gajda (3), Norbert Grząśko (4), Jakub Radocha (5), Max Bittrich (6), K. Martin Kortuem (6), Alessandro Gozzetti (7), Lidia Usnarska-Zubkiewicz (8), Iwona Hus (4), Andrew J. Yee (9), David S. Jayabalan (10), Ruben Niesvizky (10), Julia Kelman (10), Daniel Coriu (11), Laura Rosiñol (12), Łukasz Szukalski (13), Julio Davila (14), Veronica González-Calle (14), Krzysztof Jamroziak (15), Irit Avivi (16), Yael Cohen (16), Anna Suska (1), Aimee Chappell (17), Deepu Madduri (18), Saurabh Chhabra (19), Ariel Kleman (19), Parameswaran Hari (19), Sebastian Grosicki (20), Paweł Robak (21), Massimo Gentile (22), Izabela Kozłowska (23), Stuart L. Goldberg (24) and David H. Vesole (25)

(1) Department of Hematology, Jagiellonian University Medical College, Cracow, Poland; (2) Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA; (3) Department of Hematology, Oncology and Internal Diseases, Warsaw Medical University; (4) Department of Haematology and Bone Marrow Transplantation, Medical University of Lublin, Lublin, Poland; (5) 4th Department of Internal Medicine – Haematology, Faculty of Medicine in Hradec Kralove, Charles University, Czech Republic; (6) Department of Internal Medicine II, University Hospital Würzburg, Würzburg, Germany; (7) Le Scotte Hospital, Siena, Italy; (8) Department of Hematology, Blood Neoplasms and Bone Marrow Transplantation, Wroclaw Medical University, Wroclaw, Poland; (9) Massachusetts General Hospital Cancer Center, Harvard Medical School, Boston, MA, USA; (10) Weill Cornell Medical College, New York, NY, USA; (11) Department of Hematology, Fundeni Clinical Institute, University of Medicine and Pharmacy "Carol Davila", Bucharest, Romania; (12) Department of Hematology, Amyloidosis and Myeloma Unit, Hospital Clínic, IDIBAPS, University of Barcelona, Barcelona, Spain; (13) Department of Hematology, Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Toruń, Poland; (14) Hospital Universitario de Salamanca, Salamanca, Spain; (15) Institute of Hematology and Transfusion Medicine, Warsaw, Poland; (16) Tel Aviv Medical Center, Tel Aviv, Israel; (17) Medstar Georgetown University Hospital Department of Hematology/Oncology, Washington, NW, USA; (18) Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai, New York, NY, USA; (19) Division of Hematology/Oncology Department of Medicine Medical College of Wisconsin, Milwaukee, WI, USA; (20) Medical University of Silesia, Katowice, Poland; (21) Medical University of Lodz, Lodz, Poland; (22) Division of Haematology, Dipartimento di Biotecnologie Cellulari et Ematologia, University La Sapienza, Rome, Italy; (23) Department of Hematology, SPZOZ ZSM in Chorzow, Poland; (24) John Theurer Cancer Center at Hackensack UMC, Hackensack, NJ, and Cota Inc., New York, NY, USA; (25) John Theurer Cancer Center at Hackensack UMC, Hackensack, NJ, USA

INTRODUCTION

Intrinsic genetic abnormalities in malignant plasma cells are one of the strongest predictive factors in multiple myeloma (MM) patients. The presence of t(14;16)(q32;q23) is associated with deregulation of the c-musculoaponeurotic fibrosarcoma (c-MAF) oncogene. Due to the relative rarity of t(14;16) [<5% of newly diagnosed MM], there are no large databases constituting a source of information about the natural history of this abnormality (the largest reported by Palumbo et al.*, *R-ISS for MM: An IMWG Report* included 84 patients).

METHODS

We retrospectively analyzed 213 patients with t(14;16) from 24 clinical centers in Germany, Italy, Spain, Israel, Poland, Romania, Czech Republic and the United States. The diagnosis and clinical responses were based on the International Myeloma Working Group criteria. The t(14;16) was detected by double color fluorescence *in situ* hybridization using bone marrow samples. Baseline characteristics at diagnosis, patient treatment and clinical outcomes were collected using unified forms. The study was approved by institutional review boards. Progression-free survival (PFS) was defined as the period between the date of diagnosis and either the date of the first relapse, or the last observation or death from any cause. Overall survival (OS) was defined as the period between the date of diagnosis and the date of death or last observation. Cox proportional hazard regression analysis was applied to assess risk factors of death. Survival curves were plotted by the Kaplan-Meier method and compared using log-rank and Breslow-Gehan-Wilcoxon tests.

RESULTS

Patient Characteristics

We analyzed a total of 213 patients, mean age 62.1 years (range 32 to 90), including 91 (42.7%) males. Immunoglobulin isotype included IgG (n=98, 46.0%), IgA (n=60, 28.2%) and light chain only in 47 cases (22.1%). ISS stage at diagnosis included: stage I (n=47, 22.1%), stage II (n=81, 38.0%), stage III (n=78, 36.6%) and for R-ISS: stage I (n=10, 4.7%), stage II (n=71, 33.3%) and stage III (n=79, 37.1%). The stage was unknown for the remaining patients. Hypercalcaemia was present in 38 cases (17.8%), anemia (<10g/dL) in 109 (51.2%) and impaired renal function (creatinine clearance <40 mL per minute or serum creatinine >2 mg/dL) in 54 (25.4%) patients. In 104 (48.8%) cases, osteolytic lesions were present.

t(14;16)

The t(14;16) was associated with other aberrations in 134 (62.9%) cases (Table 1.), including 35 (16.4%) patients with del17p.

Treatment Modalities in Patients Positive for t(14;16)

First line treatment for MM with t(14;16) included proteasome inhibitors (PIs) +chemotherapy in 72 patients (36%), PIs + immunomodulators (IMIDs) in 39 patients (20%) and chemotherapy + PIs + IMIDs in 25 patients (13%). Responses to the treatment are presented in Table 2.

Table 1.

Additional cytogenetic abnormality	Number of patients
t(14;20)	4 (1.9%)
del 17p	35 (16.4%)
RB1	1 (0.5%)
trisomy 15	4 (1.9%)
gain 1q21	69 (32.4%)
del 13q14	65 (30.5%)
t (6;14)	6 (2.8%)
t (4;14)	29 (13.6%)
t (11;14)	23 (10.8%)
IgH disruption	43 (20.2%)

Table 2.

Responses	Response after 1. line of treatment n=159
Complete remission	46 (28.9%)
Very Good Partial Remission	47 (29.6%)
Partial Remission	46 (28.9%)
Minimal Response	4 (2.5%)
Stable Disease	7 (4.4%)
Progressive Disease	9 (5.7%)

Survival

Overall response rate was 67%. Median PFS was 31 months (95% CI 28-40.3 months, Figure 1.). Median OS was 88 months (95% CI 49-177 months, Figure 2.). 5-year OS from MM diagnosis was 55% (95% CI 46-63%), and 10-year OS was 44% (95% CI 31-56%). For stage I median PFS was 41 months (95% CI 29-54 months), median OS for stage I was not reached. For stage II median PFS was 92 months (95% CI 22-177 months) and median OS was 62 months (95% CI 38-177 months). For stage III median PFS was 18 months (95% CI 12,4-28 months) and median OS was 32 months (95% CI 18-88 months; Figure 3 and 4; in *Palumbo et al.* study* for stage I R-ISS: median PFS= 66 months , median OS= not reached; for stage II R-ISS median PFS= 42 months , median OS= 83 months and for stage III R-ISS median PFS= 29 months and median OS= 43 months). Patients in ISS stage I had better OS than stage III patients (p<0.001). Patients with additional del17p (double hit myeloma) exhibited worse OS than patients with single t(14;16) mutation (median OS 42 vs. 107 months, p=0.043, Figure 5.). A total of 74 (34.7%) patients died. The causes of death included mostly disease progression in 28 cases (37.8%; 16 patients received ≥4 treatment lines) and infection in patients with progression in 21 cases (28.4%).

Patients treated with combined therapy with IMIDs, PIs chemotherapy had better survival than patients treated with IMIDs or PIs alone or chemotherapy alone (p=0.044, Figure 6). Patients after auto-PBSCT (median OS not reached, n=62, 29.1%), especially tandem auto-PBSCT (median OS not reached, n=18, 8.5%) had better OS than patients without transplant (median OS 42.1 months, 95% CI 27-62 months, p<0.0001, Figure 7.).

Figure 1. Progression-free survival

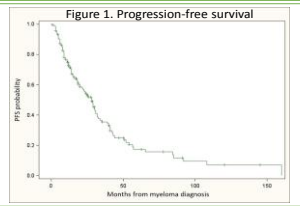


Figure 2. Overall survival

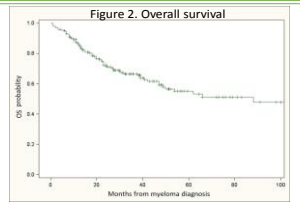


Figure 3. OS according to ISS stage

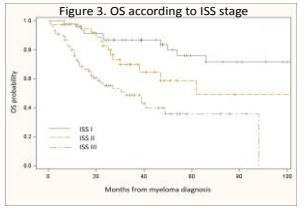


Figure 4. PFS according to ISS stage

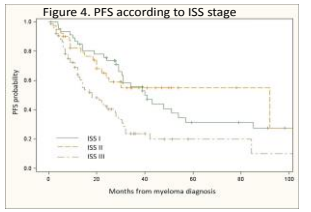


Figure 5. OS according to del17p status

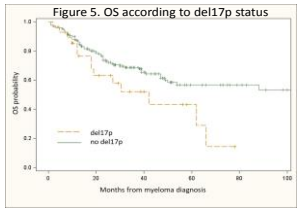


Figure 6. OS according to treatment

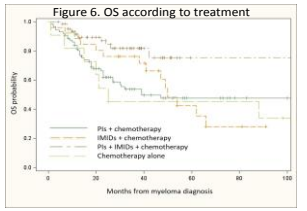
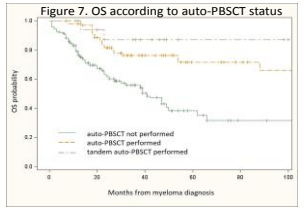


Figure 7. OS according to auto-PBSCT status



CONCLUSION

This is the largest report of myeloma patients with t(14;16). Patients with isolated t(14;16) had better prognosis than those with t(14;16) and del17p. The use of auto-PBSCT, especially in patients who received planned tandem auto-PBSCT, was associated with better survival. Combined therapy with PIs and IMIDs improved OS in t(14;16) patients, which may suggest that this high-risk prognostic feature might be partially overcome by the use of new drug therapies. This study of 213 patients indicates that t(14;16) is not as unfavorable factor as shown in the original IMWG R-ISS analysis (n= 84); this may be the result of higher numbers of patient in our study being treated with combinations of IMiDs and PIs. Regardless, this data suggests that the revised ISS may require updating.

*Palumbo et al. Revised International Staging System for Multiple Myeloma: A Report From International Myeloma Working Group. J Clin Oncol. 2015;33:2863-9.

Hematogenous Extramedullary Relapse (HEMM) in Multiple Myeloma - A multicenter Retrospective Study in 127 patients

Irit Avivi(1), Yael Cohen(1), Gabor Mikala(2), Laurent Garderet(3), Mor Seny Gueye(3), Sophia Glickman(4), David S. Jayabalan(4), Ruben Niesvizky(4), Alessandro Gozzetti(5), Katarzyna Wiśniewska-Piąty(6), Anna Waszczuk-Gajda(7), Lidia Usnarska-Zubkiewicz(8), Iwona Hus(9), Renata Guzicka(10), Jakub Radocha(11), Vibor Milunovic(12), Julio Davila(13), Massimo Gentile(14), Anna Suska(15), Sarah Goldman-Mazur(15), Jorge J. Castillo(16) and Artur Jurczyszyn(15)

(1) Tel Aviv Medical Center, Tel Aviv, Israel,(2) Department of Hematology and Stem Cell Transplantation, South-Pest Central Hospital, Natl. Inst. Hematol. Infectol., Budapest, Hungary, (3) Service d'Hématologie et thérapie cellulaire, Hôpital Saint Antoine, Paris, France, (4) Weill Cornell Medical College, New York, NY, USA, (5) Le Scotte Hospital , Siena , Italy, (6) Department of Haematology ,Silesian Medical University, Katowice, Poland.,(7) Department of Hematology, Oncology and Internal Diseases, Warsaw Medical University, (8) Department of Hematology , Blood Neoplasms, Wroclaw Medical University , Wroclaw , Poland.,(9) Department of Haematology ,Bone Marrow Transplantation , Medical University of Lublin , Lublin , Poland,, (10) Department of Haematology, Pomeranian Medical University, Szczecin, Poland,(11) 4th Department of Medicine – Haematology, Charles University Hospital Hradec Kralove, Hradec Kralove, Czech Republic, (12) Division of Hematology , Clinical Hospital Merkur , Zagreb , Croatia. 13) Hospital Universitario de Salamanca, Salamanca, Spain,(14) Hematology Unit, Department of Onco-Hematology, A.O. of Cosenza, Cosenza, Italy,(15) Department of Hematology, Jagiellonian University Medical College, Cracow, Poland, (16) Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA

BACKGROUND

Hematogenous Extramedullary myeloma (HEMM), defined by the presence of plasma cells (PCs) outside the bone marrow, is reported in 10% to 30% of patients during the disease course.

OBJECTIVES

The current study was aimed to evaluate the clinical characteristics and prognostic factors, including the impact treatment sequencing since diagnosis, on the outcome of patients diagnosed with HEMM relapse and define the best treatment approach

METHODOLOGY

It was retrospective analysis in 16 Centers in 127 patients with HEMM. Patients from below cities were analysed: Kraków, Warszawa, Wrocław, Wałbrzych, Katowice, Lublin, Szczecin, Hradec Kralove, Paris, Zagreb, Budapest, Siena, Cosenza, Salamanca, New York and Tel Aviv.

.

Inclusion criteria
Age > 18 years
Available data on all treatment lines from the diagnosis of MM, including response to treatment
Data on HEMM, including time and organ involvment
Available data on HEMM treatment

The study focus on:
-OS
-Response to HEMM treatment (quality and duration)
-HEMM risk factors
-Risk factors for death in the course of HEMM

RESULTS

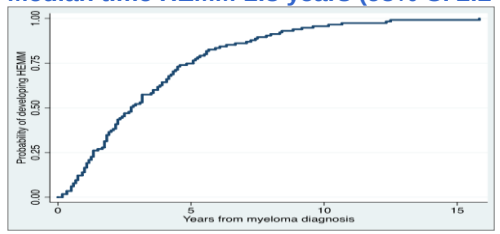
Patient characteristics at diagnosis

Characteristic	Median (range) or N (%)
Age (continuous) (n=127)	63 (31-94)
Male sex (n=127)	76 (60%)
IIMM (n=127)	91 (72%)
LCMM	29 (23%)
Non-secret	7 (6%)
IgG (n=120)	59 (50%)
IgA	31 (26%)
IgD	1 (0.8%)
Other	1 (0.8%)
LCMM	27 (23%)
Kappa (n=119)	69 (58%)
Albumin (continuous) (n=114)	37 (20-60)
Beta-2-micro (continuous) (n=110)	4.2 (0.6-36.8)
ISS1 (n=117)	35 (30%)
ISS2	31 (27%)
ISS3	51 (44%)
t(4;14) (n=88)	17 (19%)
t(14;16)	2 (2%)
t(14;20)	0 (0%)
Del17p	10 (11%)
Del13q	28 (32%)
t(11;14)	6 (7%)
CD56 (n=46)	33 (72%)
CD20 (n=37)	6 (16%)
IMID 1L (n=127)	70 (55%)
Proteasome inhibitors 1L	70 (55%)
Chemotherapy 1L	79 (62%)
ASCT 1L (n=126)	74 (59%)
Plasmacytomas at dx (n=127)	73 (57%)

Patient characteristics at HEMM relapse

Characteristic	Median (range) or N (%)
Pure HEMM (n=123)	47 (38%)
HEMM with paraspinal masses	76 (62%)
BM involvement (n=98)	67 (68%)
Non- secretory (n=105)	21 (20%)
HEMM >5 cm (n=90)	38 (53%)
HEMM >2 sites (n=92)	30 (33%)
Elevated LDH	64 (59%)
CD56 (n=60)	33 (55%)
CD20 (n=59)	8 (14%
0 prior lines (n=127)	13 (10%)
1 prior line	37 (29%)
2+ prior lines	77 (61%)
IMID (n=127)	50 (39%)
Proteasome inh	64 (50%)
MAB	13 (10%)
Chemotherapy	67 (53%)
CR to therapy (n=116)	17 (15%)
VGPR	15 (13%)
PR	25 (22%)
SD/PD	59 (51%)

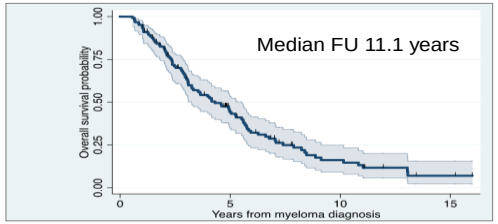
Median time HEMM-2.8 years (95% CI 2.2-3.6).



Factor predicting shorter time to HEMM

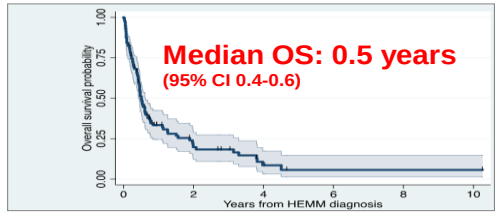
B2M levels, del17p and plasmacytomas at diagnosis predict shorter duration & upfront ASCT predicts a longer period to HEMM disease

Overall survival from MM diagnosis

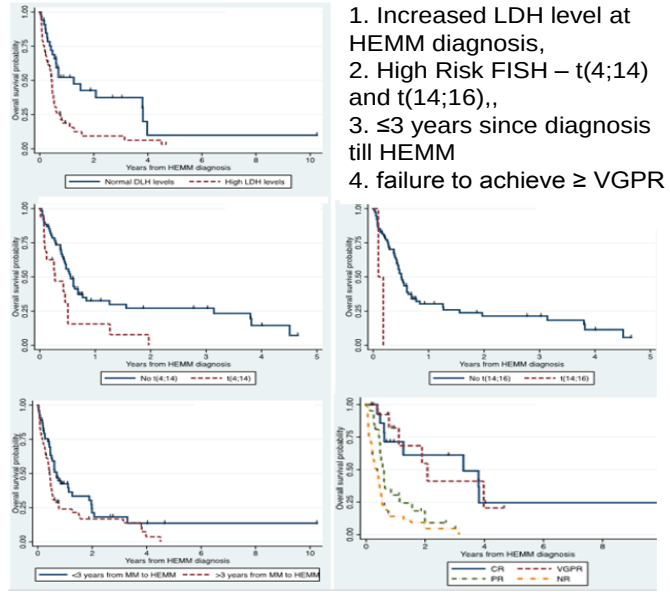


Median OS 4.3 years (95% CI 3.3-5.5

Overall survival from HEMM



Factors Predicting shorter OS at HEMM relapse



1. Increased LDH level at HEMM diagnosis,
2. High Risk FISH – t(4;14) and t(14;16),,
3. ≤3 years since diagnosis till HEMM
4. failure to achieve ≥ VGPR

CONCLUSIONS

In MM patients who develop HEMM, the median time from MM to HEMM diagnosis is 2.8 years. Despite the improvement in MM therapy over the last decades, patients with HEMM diagnosis have a dismal outcome. Median OS from HEMM is only 6 months. Further studies assessing best therapy in patients experiencing this complication are warranted.

Abstract #1980

MP0250 COMBINED WITH BORTEZOMIB AND DEXAMETHASONE IN MULTIPLE MYELOMA PATIENTS PREVIOULSY EXPOSED TO PROTEASOME INHIBITORS AND IMMUNOMODULATORY DRUGS

Stefan Knop[1], Hartmut Goldschmidt[2], Marc. S. Raab[2], Monika Szarejko[3], Artur Jurczyszyn[4], Jan Duerig[5], Sara Bringhen[6], Barbara Gamberi[7], Angelo Vacca[8], Jorge Acosta[9], Guy Lemaillet[9], Cédric Cortijo[9], Sudhir Bansod[9], Norbert Grzasko[10].

[1]Department of Medicine II, University Hospital Wurzburg, Germany, [2]Department of Hematology, Oncology, and Rheumatology, Heidelberg University Hospital, Germany, [3]University Clinical Centre, Department of Hematology and Transplantology Gdansk, Poland, [4]University Hospital, Clinical Department of Hematology, Krakow, Poland, [5]Department of Hematology, University Hospital Essen, Germany, [6]Department of Oncology and Hematology, Clinical trials in onco-hematology and multiple myeloma, City of Health and Science of Turin, Italy, [7]Hematology Complex Operative Unit, Senior Hospital Santa Maria Nuova, Reggio Emilia, Italy, [8]Department of Biomedical Sciences and Human Oncology, Section of Internal Medicine, University of Bari Medical School, Bari, Italy, [9]Molecular Partners AG, Zürich, Switzerland, [10]Department of Hematology, Centre of Oncology of the Lublin Region, Poland.

MOLECULAR partners

MP0250 Mechanism of Action

MP0250 is a first-in-class selective tri-specific multi-DARPin® drug candidate neutralizing VEGF-A and HGF as well as binding to human serum albumin to increase its plasma half-life. Preclinical studies have shown that MP0250 enhances sensitivity of Multiple Myeloma (MM) cells to bortezomib, inhibits tumour growth and reduces bone destruction[1].

In this clinical phase 2 trial (NCT03136653), we are investigating the safety, tolerability and efficacy of the combination of MP0250 plus bortezomib and dexamethasone (dex) in patients (pts) with relapsed/refractory (RR) MM previously exposed to proteasome inhibitors (PI) and immunomodulatory drugs (IMiD) (Figure 1).

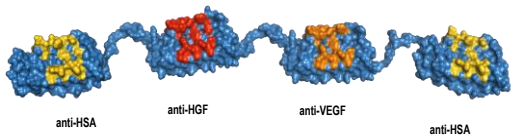


Figure 1. Model of MP0250 with binding surfaces in colour.

MP0250-CP201 Study Design

This study is a Phase II open-label, single-arm, multicenter trial of MP0250 plus bortezomib and dexamethasone in patients with relapsed/refractory multiple myeloma containing a dose escalation (Part 1) and expansion (Part 2) part.

This trial is recruiting adults ≥18 years of age with RRMM who have progressed after at least two prior treatment regimens including bortezomib and an IMiD. A dose-escalation phase (part 1) consisting of two cohorts will define a safe dose of the combination of MP0250 plus bortezomib + dex followed by a dose-expansion phase (part 2).

Patients were enrolled to receive iv MP0250 on day 1 + subcutaneous bortezomib 1.3 mg/m² on days 1, 4, 8, 11, oral dexamethasone (dex) 20 mg on days 1-2, 4-5, 8-9, 11-12 of each 21-day cycle. Up to 40 patients will be enrolled. Patients will receive treatment until there is documented disease progression or unacceptable toxicity.

Study MP0250-CP201 (NCT03136653) is being conducted at 9 centres in three European countries (Germany, Italy and Poland).

Methods

Eligible patients were aged ≥ 18 years with an Eastern Cooperative Oncology Group performance status of ≤ 1 and documented diagnosis of RRMM with measurable disease by serum M protein ≥0.5 g/dL or urine M protein ≥200 mg/24 h electrophoresis. Patients were ineligible if the previously have peripheral neuropathy ≥ 2 or a history of active congestive heart failure, myocardial infarction within 6 months prior to screening and/or uncontrolled hypertension.

The primary endpoint is efficacy in terms of overall response rate (ORR) per International Myeloma Working Group criteria. Secondary endpoints include safety, immunogenicity, progression free survival, and duration of response. Exploratory endpoints include overall survival and pharmacokinetics. The safety analysis set is defined as patients who have received at least 1 dose of the combination of MP0250 plus bortezomib + dexamethasone.

Patients and treatments

Data cut off was 02 November 2018. 8 pts have been treated in cohort 1 (8 mg/Kg q3w) and 3 pts in cohort 2 (12 mg/Kg q3w). Part 2, is currently open and recruiting patients to receive 8 mg/kg q3w. At cut-off date, two patients have been enrolled in part 2.

Table 1. Patient demography and baseline characteristics

Demographics	Part 1 Escalation		Part 2 Expansion
	Cohort 1 (8 mg/Kg) n = 8	Cohort 2 (12 mg/Kg) n = 3	8 mg/Kg n = 2
Median age (y)	57.75	55.66	62
Gender (F/M)	4 / 4	2 / 1	2 / 0
ECOG, n (%) 0	4	2	1
1	4	1	1
B2-microglobulin (mg/L) Median (range)	3.65 (2.2-6.9)	3.36 (2.5-5.1)	2.35 (1.6 – 3.1)
Haemoglobin (g/L) Median (range)	120.5 (95-143)	121.66 (101-134)	117 (97-137)
Platelets, $x10^9$/L Median (range)	181.1 (72-327)	153.6 (111-219)	245.5 (146-345)
ANC, $x10^9$/L Median (range)	2.68 (1.3-4.4)	3.03 (2.3-3.8)	2 (1.3-2.7
Median prior lines of treatment (range)	3.25 (2-5)	3.5 (3-5)	4.5 (3-6)
Time from initial diagnosis (y) Median (range)	4.7 (1.3-10)	5.5 (2.5-9)	10 (8-12)
PI Refractory , n (%)	4 (50%)	3 (100%)	1 (50%)
Prior SCT, n (%)	7 (87.5%)	3 (100%)	2 (100%)

Table 2. Patient Disposition

	Part 1: Dose Escalation		Part 2: Expansion
	Cohort 1: 8 mg/Kg (n =8)	Cohort 2: 12 mg/Kg (n = 3)	8 mg/Kg (n = 2)
On treatment, n (%)	1	0	2
Discontinued, n (%)			
PD	4	2	0
Consent withdrawn	1	0	0
AE	2	1	0
Death	0	0	0

Table 3. Treatment Emergent Adverse Event reported (N=11)

Most common adverse events during treatment				
Adverse Event	Part 1: Dose escalation			
	Cohort 1: 8 mg/Kg (n=8)		Cohort 2: 12 mg/Kg (n=3)	
	Any Grade	Grade ≥ 3	Any Grade	Grade ≥ 3
Hematologic adverse events				
Neutropenia	-	-	3 AE (1 pt.)	2 AEs (1 pt.)
Thrombocytopenia	4 AEs (3 pts.)	1 AE (1 pt.)	12 AEs (3 pts.)	8 AEs (3 pts.)
Anaemia	-		8 AEs (2 pts.)	4 AEs (2 pts.)
Non-hematologic adverse events				
Epistaxis	-	-	5 AEs (1 pt.)	-
Peripheral Sensory Neuropathy	2 AE (1 pt.)	-	1 AE (1 pt.)	-
Hypertension	5 AEs (5 pts.)	3 AE (3 pt.)	3 AEs (3 pt.)	1 AE (1 pt.)
Proteinuria	1 AE (1 pt.)	1 AE (1 pt.)	2 AEs (2 pt.)	1 AE (1 pt.)
Nausea	1 AE (1 pt.)	1 AE (1 pt.)	3 AEs (1 pt.)	-
Respiratory tract infection	1 AE (1 pt.)	1 AE (1 pt.)	1 AE (1 pt.)	-
ALT elevation	2 AEs (1 pt.)	1 AE (1 pt.)	-	-
AST elevation	1 AE (1 pt.)	-	-	-
GGT elevation	1 AE (1 pt.)	1 AE (1 pt.)	-	-
Diarrhoea	-	-	1 AE (1 pt.)	-

- No AEs reported in 2 patients enrolled in Part 2 Expansion phase (8 mg/kg) at data cut-off.
- The most frequent drug-related grade ≥ 3 AEs: hypertension in 4 pts, thrombocytopenia in 4 pts, proteinuria in 2 pts and transient liver enzyme elevation in 1 patient.
- One dose-limiting toxicity has been reported in cohort 1 (grade 3 hypertension) and two in cohort 2 (grade 3 epistaxis, grade 3 proteinuria).

Pharmacokinetics and Immunogenicity

Figure 2. Concentration time profile for MP0250 in cohort 1 patients (≥ 3 doses) [n = 7]

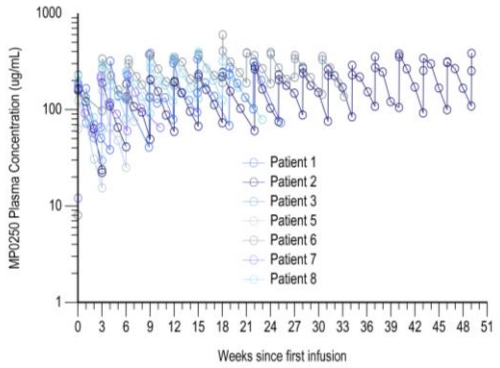
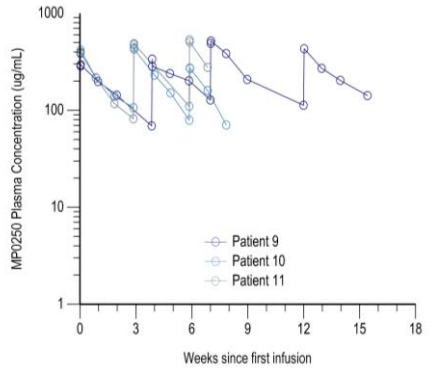


Figure 3. Concentration time profile for MP0250 in cohort 2 patients [n = 3]



- Repeated MP0250 dosing led to sustained drug exposure throughout the treatment periods analysed, the longest to-date being 12 months; increase in MP0250 exposure between cohort 1 and cohort 2 is proportional with dose increase.
- MP0250 in combination with bortezomib and dexamethasone has a half-life of ca. 11 days (range: 6-17 days) and shows only slight accumulation upon repeated dosing (factor 1.4-3.1 based on Cmin, CMax, and AUC); pharmacokinetics are similar to those previously observed with single agent administration of MP0250
- All 11 patients in the dose-escalation portion were assessed for anti-drug antibody (ADA) formation; 2 patients were found to be ADA positive with very low and stable titer (range 1-4) and no impact on PK profile or exposure to MP0250.

Efficacy

All 11 patients in the dose escalation portion were evaluable for tumour response (Fig.5). The ORR (better than or equal to PR) for all treated patients was 45.5%.

Figure 4. Response outcomes

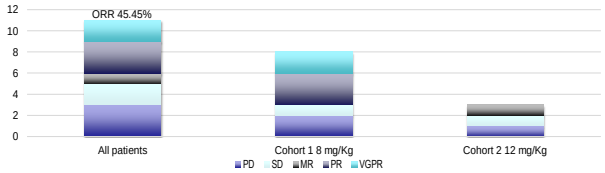
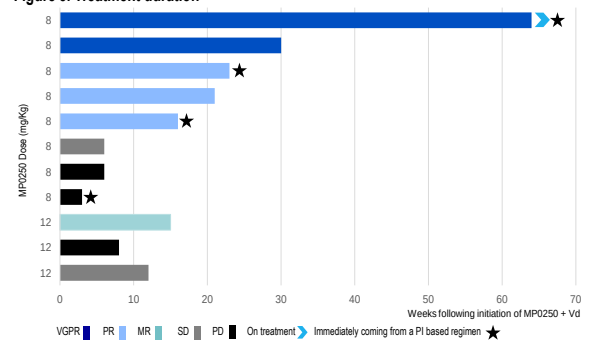


Figure 5. Treatment duration



- Tree out of four patients who were coming immediately from a PI based regimen achieved a response. One patient has been on treatment longer than 12 months and achieved VGPR.
- Follow-up in Part 2 is very short a data cut-off.

Conclusions

Data from cohort 1 (8 mg/Kg q3w) suggest that MP0250 can be safely combined with bortezomib and dex in patients with relapsed and refractory MM.

Durable responses were seen in patients who came from PI based pre-treatment suggesting that MP0250 has the potential to overcome the adaptive PI resistance mechanism

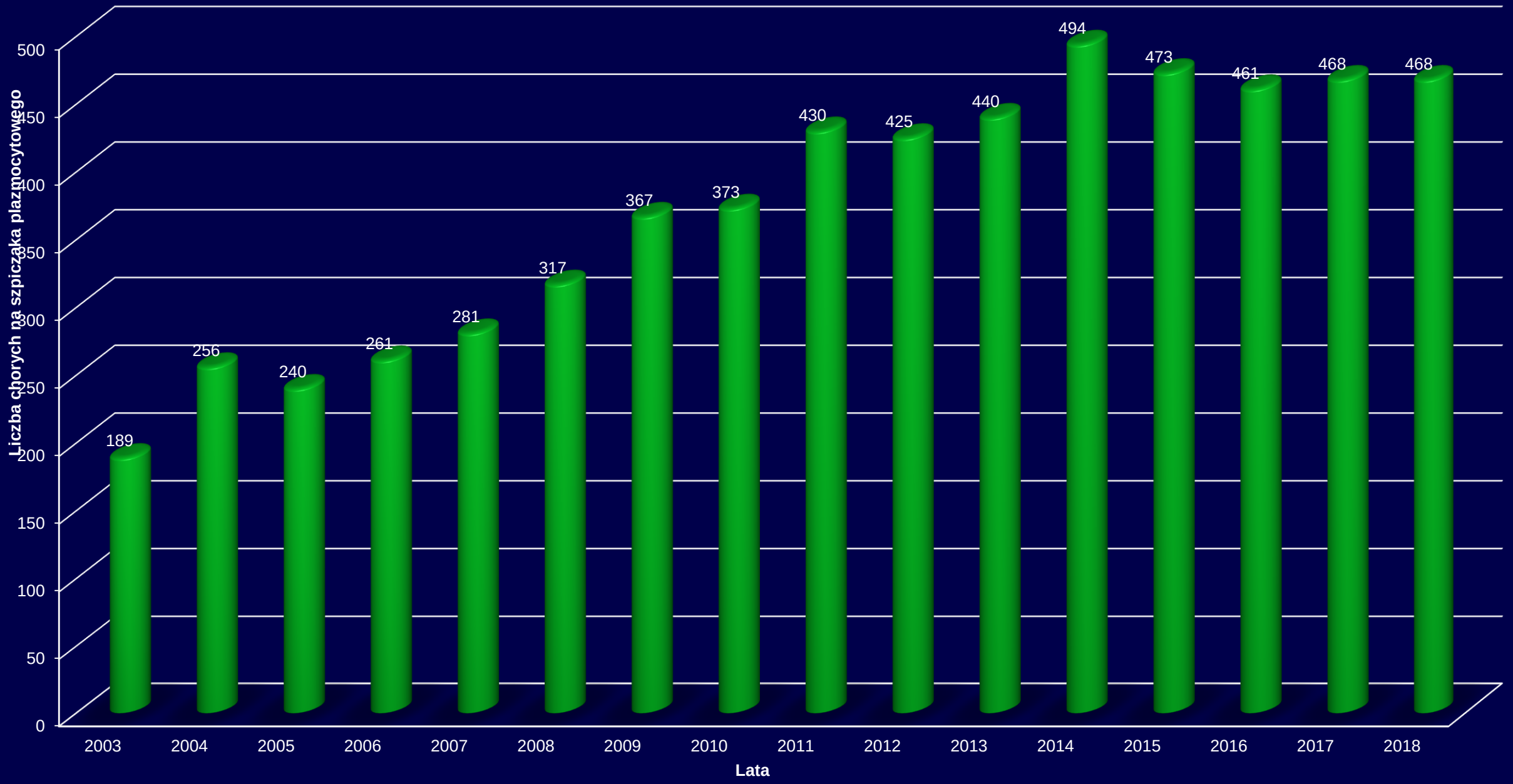
Acknowledgment

We thank the patients and families who contributed to this study, as well as the study investigators, nurses and clinical research personnel from the study centres across Europe. This study is sponsored by Molecular Partners AG.

References

1) Fiedler U, Ekawardhani S, Cornelius A, et al. Targeting angiogenesis in multiple myeloma by the VEGF and HGF blocking DARPin protein MP0250: a preclinical study. Oncotarget. 2017;8(58):98371-83.

Liczba chorych na szpiczaka plazmocytowego w Klinice Hematologii UJ CM w latach 2002-2018



Procedury Auto i Alotransplantacji
wykonane na Oddziale Przeszczepiania Szpiku Kostnego SU w latach 1998 – 2018

	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	Suma
Auto	26	27	31	28	36	34	32	34	40	37	37	44	59	70	53	58	46	32	37	56	82	899
Allo		6	10	8	8	21	17	15	9	8	18	17	12	9	22	21	14	11	16	15	16	273
MUD														1		9	29	35	25	22	31	121
HAPLO																		3	1	2	4	10
DLI																		4	1	4	-	9
Łącznie	26	33	41	36	44	55	49	49	49	45	55	61	71	80	75	88	89	78	78	93	133	1328

Liczba transplantacji w latach 1998 – 2018 z uwzględnieniem diagnozy

	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	Łącznie z daną diagnoza
ALL	4	4	7	2	4	3	3	4	10	3	3	3	3	1	5	5	6	7	4	11	11	103
AML	11	6	13	6	9	13	11	5	1	4	9	8	4	11	9	14	26	27	27	15	21	250
MM	3	4	6	4	8	5	5	11	11	10	10	17	30	36	29	38	26	17	20	41	50	**381**
NHL	3	4	4	5	8	15	13	17	9	18	20	21	15	11	2	3	2	2	4	6	13	195
CML	2	6	4	3		5	2	2	2	1	4	1	2	1	1	-	-	1	1	2	3	43
HD		6	3	7	11	8	7	7	16	7	5	5	11	7	8	7	5	8	10	5	8	151
DLBCL				3		3	1					3	1	3	6	4	8	8	1	0	7	48
SAA				2		1	2	1		2			2		2	1	2	1	3	3	1	23
CLL				1		1	1	2					1		2	2	2	1	-	-	-	13
MCL					1		1				2			8	5	3	6	2	1	5	7	41
PML						1							1	2	1	1	-	-	-	-	-	6
PNH											1				2		1	1	-	-	-	5
MDS											1	2	1		2	3	3	-	5	3	6	26
OMF												1				4	2	2	2	1	5	17
CMML																		1				1
POEMS																				1	1	2
Inne	3	3	4	3	3	-	3	-	-	-	-	-	-	-	-	3	-	-	-	-	-	22

Przyszłe standardy terapii nowo rozpoznanych starszych chorych ze szpiczakiem plazmocytowym

MPV → MPV + DARA — ALCYONE (NCT 02195479)

Rd →
- V + Rd — SWOG SO777
- Elo + Rd — ELOQUENT-1 (NCT 01335399)
- Dara + Rd — MAIA (NCT 02252172)
- Ixa + Rd — TOURMALINE MM2 (NCT 01850524)
- Isa + VRd — IMROZ (NCT 03319667)
- Dara + VRd — CEPHEUS

MP- melfalan, prednisone; MPV- melfalan, prednisone, bortezomib
Dara- daratumumab ; Elo- elotuzumab ; Ixa- ixasomib,
Isa - isatuximab ; Rd- lenalidomid, dexametazon

PTH.T

FUNDACJA CENTRUM LECZENIA SZPICZAKA

VIII Myeloma and Lymphoma International Conference in Kraków 2019

(former "Complex treatment of plasma cell dyscrasia")

6-7 th September 2019

LOCATION: Jagiellonian University Medical College, Św. Anny 12, 31-008 Krakow

UNIWERSYTET JAGIELLOŃSKI COLLEGIUM MEDICUM

Szpital Uniwersytecki w Krakowie

Małopolska

KRAKÓW krakow.pl

September 7 2019

13.00 - 13.10 assoc. prof. **Artur Jurczyszyn** and prof. **Wojciech Jurczak**
Jagiellonian University Faculty of Medicine Department of Hematology, Kraków – opening the conference

13.10 - 13.15 prof. **MACIEJ MAŁECKI**
Dean of Faculty of Medicine Jagiellonian University Medical College, Kraków - opening the conference

13.15 - 13.45 prof. **MERAL BEKSAC**
Department of Hematology, Ankara University, Ankara, Turkey
„Multiple myeloma – the best therapy for newly diagnosed patients in 2019"

13.55 - 14.25 prof. **JOSEPH MIKHAEL**
Professor, Applied Cancer Research and Drug Discovery Translational Genomics Research Institute (TGen), City of Hope Cancer Center; Chief Medical Officer, International Myeloma Foundation; Adjunct Professor, Arizona State University, College of Health Solutions
„Therapy of relapsed/refractory multiple myeloma in 2019"

14.35 - 15.05 prof. **JOAN BLADE**
Department of Hematology, Hospital Clínic de Barcelona, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Spain
„Amyloidosis and POEMS – how I treat in 2019"

15.15 - 15.45 prof. **SUZANNE LENTZSCH**
Division of Hematology/Oncology, Columbia University Medical Center, Herbert Irving Pavilion, 161 Fort Washington Ave, New York, NY, 10032, USA
„The critical role of the imaging in the management of multiple myeloma"

COFFEE BREAK until 16.20

16.20 - 16.50 prof. **SAGAR LONIAL**
Emory University, Atlanta, GA, USA
„CAR-T cells and immune system in multiple myeloma"

17.00 - 17.30 prof. **PETER BORCHMANN**
Department of Hematology/Oncology at the University Hospital of Cologne, Germany
"CD19 directed CAR-T Cell Therapy in B-NHL"

17.40 - 18.10 prof. **CHRISTIAN BUSKE**
Institute of Experimental cancer Research University of Ulm, Germany
"New developments in the treatment of Waldenström's Macroglobulinemia"

18.20 - 18.50 prof. **PIERE LUIGI ZINZIANI**
University of Bologna, Italy
"The role of checkpoint inhibitors in non Hodgkin lymphoma"

19.00 - 19.30 prof. **GEORG HESS**
Universitats Medizin Mainz, Germany
"New drugs in follicular lymphoma – are we ready to skip chemotherapy"

www.szpiczak.org

Organizers: Fundacja Centrum Leczenia Szpiczaka, Katedra Hematologii UJ CM w Krakowie

www.szpiczak2019.pl