ASCO 2023-IMWG-GMAN
Jack Aiello – Terse Notes

My Key ASCO Takeaways

1) CARTITUDE-4, supporting earlier treatment, was probably the most important study for MM…LBA in ASCO, Plenary in EHA. Other CAR-T advancing manufacturing and persistence.
2) Bi-specific Antibodies (BsAb) continue to show responses in combination treatments but also experience high infection rates.
3) Additional focus on patient QoL, e.g. less dex, real world, exercise.
4) CAR-T barriers: 1) Patient-limited centers, travel, wage loss, OOP cost, Socio-Economic; 2) Provider- limited centers, logistics of post CAR-T follow-up; 3) Mfg Challenges – Slots, Long vein-to-vein time, payment/insurance

Abstracts Color Code Key
Oral: LBA, 8000-8008; Posters: All others
Green = CART, BsAb; Purple = Mass Spec/MRD; Other

LBA106 Dhakal – CARTITUDE-4 Cilta-cel vs SOC (PVd or DPd) for 1-3 LOT, Conclusion: For N=416 and ~60% HR, ORR 85% v 67%, 12 mo PFS 76% vs 49%, 10^{-5} MRD- 61% v 16%. Also better CR, PFS and MRD rates than CARTITUDE-1 given in later LOT's.

1533 Bansal – Hospital-based out-patient CAR-T and Teclistimab w remote monitoring, Conclusion: Appears feasible although numbers are small (N=39 CAR-T, 23 Tec). Fever most common cause of hospital admission.

2582 Ahlstrom – Pt perspectives CAR-T & BsAbs in RRMM, Conclusion: N=325 patients completed 18-question survey. 26% open to trying a new therapy right away and another 43% were open but wanted more information on safety and efficacy.

6574 Padnaraju – Dara-SQ infusion related reactions (IRRs), Conclusion: N=102 pts randomized to continue pre-med dex v stopping after 4th Dara-SQ dose. Since IRRs occur early, and become rare and mild over time, omitting pre-med after 4th dose is safe.

8000 Knop – KRd +/- Elo for NDMM and MRD, Conclusion: After N=525 completed 6 cycles of induction, pts ≥ VGPR and MRD- were 50% v 35%. Grade 3/4 thrombocytopenia (12% v 11%), pneumonia (8% v 6%), and grade 3/4 cardiac events (both 6%) were similar.

8001 Nooka – KPd maintenance in HRMM, Conclusion: For N=29 after SCT, ≥CR and ≥VGPR rates were 24.1% and 68.9%, respectively, which deepened to 79.3% and 100% while on study. MRD- (10^{-6} and 10^{-5}) was attained in 67% and 87% of pts. And 4-yr PFS and 4-yr OS were 54% and 67% respectively. However, the prognosis for double-hit pts (>1 high-risk factor) remains poor.

8002 Cohen – RedirecTT-1 Teclistamab (BCMA) + Talquetamab (GPRC5D) for 4+ LOT, Conclusion: For N=34 at recommended dosage Tec 3.0mg/kg + Tal 0.8 mg/kg every other week. ORR 96% (41%≥CR) is comparable to Cilta-cel. ORR 86% for EMD (1/3 of ps). CRS 74% all G1/2 but infections 79% any grade and 38% G3/4. Hoping for durability…so far 9mo PFS is 77%.

8003 Dholaria – TriMM-2 Talquetamab + Dara RRMM, at least 3 prior LOTs, Conclusion: For N=65 (many prior exposure to BCMA and CD-38 txs), steroid-sparing tal + dara showed ORR 78% with mPFS 19 mo in heavily pretreated pts with RRMM. "Relatively" low infections 72% any grade and 26% G3/4.

8004 Sperling – Ph 1 PHE885 T-charge BCMA CAR-T for RRMM ≥ LOTs, Conclusion: For N=50, high response rates (IORR 100%, CR 42%). 2 days manufacturing time so 10 days "vein-to-vein" with prolonged persistence (median 6 mos). Median time to CRS was 8 days, G1/2 86%. G3 10%.

8005 Du – Ph 1 BCMA/CD19 dual target FasTCAR-T GC012F, Conclusion: For N=29, ORR 93%, 10^{-6} MRD-100% at 6 mos, 79% at 1 yr. mPFS 38 mos. Long persistence 47% at 12 mo. 2 days manufacturing time. Median time to CRS was 6 days, G1/2 79%, G3 7%.

8006 Lee – Ph 2 LINKER-MM1 from Regeneron Linvoseltamab BCMA BsAb RRMM, Conclusion: 2 cohorts A: 50mg, N=104 and B: 200 mg, N=117 (recommended dose). ORR's were 50% and 71%, mPFS was 8 mo and Not Reached. CRS all grades and G3/4 was 55%/2% and 45%/1% respectively while infections were 62%/35% and 60%/37% respectively.

8007 Weisel – Ph 3 DREAMM-3 Belamaf vs Pd, Conclusion: N=325, 2:1 randomization, prior Rev and PI. mPFS 11.2 v 7.0 mos but not "superior" by statistical significance (hazard ratio only 1.03). ORR 41% v 36% but deeper with Belamaf (25% v 8%). Similar rates of OS and AE's, although Belamaf included eye toxicities (resolved). Study did not meet primary objective of PFS superiority.

8008 Nooka – Ph 3 MagnetisMM from Pfizer Elranatamab BsAb in prior BCMA RRMM, Conclusion: N=87, ORR 46% (prior ADC 42%, prior CAR-T 53%), mPFS 5.5 mos (4, 10), mDOR 17.1 mos (13.6, NR). Infections 74% any grade and 26% G3/4.

8009 Lin – CARTITUDE-1 Final Results, Conclusion: 3-yr results. For N=97, mPFS 35 mos. mOS Not Reached but 63% of pts alive at 3 yrs.

8010 Jian-Qing – LEGEND-2, 5 yr LCAR-B38M CAR-T, Conclusion: For N=74, 16% disease-free and alive >5 yrs. mOS 56 mos and 45% still alive.

8011 van de Donk – MajesTEC-1 Teclistamab in RRMM, Conclusion: N=165, ~2 yr follow-up. mPFS 13 mo, mDOR 24 mo (not reached for those 43% of pts achieving CR). Infections 78% any grade and 52% G3/4.

8012 Hansen – SOC Cilta-cel in RRMM, Conclusion: Real-world (RW) retrospective analysis for N=139 across 12 US medical centers vs CARTITUDE-1 trial. ORR 89% (56%) vs 98% (83%) but more HR (41% v 24%) and Extramedullary Disease (35% v 13%) (ORR w/o ED 89%/49%). 55% of RW pts would not have met CARTITUDE-1 criteria (due to low blood cells, prior BCMA, organ dysfunction, PCL…).

8060 Joseph – Exercise and T-cell exhaustion in MM, Conclusion: N=24 pts participated in 6-mos physical activity intervention (strength training, walking 12 pts each). Physical activity rendered less exhausted T cell (examined CD4 and CD8 markers of exhaustion).

Global Myeloma Action Network (GMAN)

The mission of GMAN (Global Myeloma Action Network) is to improve the lives of myeloma patients around the world. Founded in 2013 by the IMF (International Myeloma Foundation), GMAN is a group of myeloma patient organizations around the world who share best practices that address mutual areas of concern such as access to drugs/treatments and awareness of myeloma. This year, GMAN was attended by 40 advocates representing 5 continents and 30 countries. The meeting was facilitated by Serdar Erdogan, Myeloma advocate from Turkey, and Director of GMAN, and Yelak Biru (CEO and President of IMF).

Opening and Closing Keynote presentations were given Drs Brian Durie and Harmut Goldschmidt (Germany) respectively. Additionally, some of the pharma sponsors (BMS, Sanofi, Pfizer and Janssen) gave talks.

GMAN broke into working group in order to develop goals, outcomes and action items for the following working groups:

1) Access to Care
2) Capacity Building
3) Health Policy
4) Clinical Research (I'm a co-chair for this group)

Finally, one of the outstanding events during our annual GMAN meeting is to hear from recipients of last year's Susie Novis Durie grants and the announcement of this year's winners. I was quite touched by Turkey's 2023 grant project focusing on Myeloma patients caught in their recent earthquake. What's a patient to do when roads to the local hospital are inaccessible and then they learn that the hospital has been flattened to the ground?

International Myeloma Working Group (IMWG)

The IMWG, founded by the IMF in 2009, consists of 300 Myeloma experts, of which 100 were invited to attend this 14th annual meeting in Europe, typically scheduled around the European Hematology Association (EHA) conference, similar to the ASH meeting in the US. The IMWG actually meets twice a year (ASH-morning breakfast, EHA- 2 days) to collaborate on myeloma projects that will benefit both patients and physicians who treat them. At this meeting, the IMWG Chairmen were Drs. Brian Durie (IMF co-founder), S. Vincent Rajkumar (Mayo), Philippe Moreau (France), Nikhil Munshi (Dana Farber) and Jesus San Miguel (Spain), an impressive group of world-wide MM experts.

Presentations and active discussions were held on the following working groups:

1) MGUS & Smoldering MM
2) MRD & Mass Spectrometry
3) Bone Disease
4) Frontline Therapy
5) Early Relapse Management
6) Immunotherapy

Some provocative remarks (and author, if known) included:

“Is MGUS a disease of condition?” patient of JS Miguel

“Screening is not yet recommended”

“CTC (Circulating Tumor Cells) > .2% have ultra high risk progression to MM. “ MV Mateos

“If SMM is treated, are they considered Newly Diagnosed MM or on their 2nd LOT for future clinical trial enrollment?” N Munshi

“Blood Flow and Mass Spec can replace a Bone Marrow Biopsy as sensitivity increases.” N Puig. “Mass “Spec will replace SPEP and IFE.” S Kumar

“Getting to 1 yr sustained MRD is critical” N Munshi

“Is MRD- after 4 cycles of induction the same as MRD- after induction->SCT-> 1 yr maintenance?” JS Miguel. [N Munshi answered “Yes”; S Lonial argued “You should still complete the treatment plan in order to achieve sustained MRD-.”

“If we’re able to cure MM with SCT or CAR-T, we still need to understand the biology of the disease at the end of those treatments.” P Voorhees

“If a pt starts with Velcade and relapses, he’ll get Kyprolis; but if a patient starts with Kyprolis, he never sees Velcade.” P Voorhees

“The biggest challenge is to treat patients who relapse < 1yr after their first line of treatment.” M Dimopoulus

“For short responses to DRd, think PI (Velcade of Kyprolis); for long responses, think Pom.” S Lonial

“In the US, 35K MM dx’s per year and 10K transplants per year.”

“How dose Bone Disease correlate with PFS and OS as a prognostic value?” E Terpos

“There are so many CAR-Ts and Bi-specifics but we’re still at the beginning of completely understand immunotherapy.” T Martin & A Chari [Dr Ajai Chari becomes chair at UCSF August 1, 2023]

“One size doe NOT fit all.” T Martin; “When will I know what size is best for me?” J Aiello

Finally, one of the highlights of this meeting is the dinner and presentation of the winners of the 2023 Robert Kyle and Brian Durie Awards. The winners respectively were Dr Maria-Victoria Mateos (Spain, 1st woman to be honored with this award) and Dr Thomas Martin (UCSF, “toasted and roasted” by Dr Jeff Wolf).