

IMS 2022, Los Angeles, Aug 25-27, 2022
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This is my fifth time attending an International Myeloma Society (IMS) conference (previously referred to as International Myeloma Workshop) which used to meet every other year but now meets every year. According to IMS president Dr Nikhil Munshi, “about 1600 folks attended in person and thousands more virtually.” Many countries are represented by myeloma specialists together with nurses, pharma reps, and a few patients. This was the 19th IMS meeting, which like ASH, also has exhibitors and posters but the focus is very much on the oral presentations and the topic is always Myeloma. The first IMS meeting was held in 1986 with 33 attendees (including Drs Robert Kyle and Brian Durie).

After the section below, I’ve organized this paper somewhat along the same lines as the conference was presented. I’ve presented the highlight without a lot of detail but included the speaker at the end (typically the principal investigator). If you follow me on Twitter (@JackMAiello) I posted a number of detailed tweets during the meeting. I apologize up front for all the shorthand initials and abbreviations with no glossary, but there are some very good glossaries available (see <https://www.myeloma.org/publications-videos/terms-definitions-multiple-myeloma>).

Quotes and Notes

- 1) During the meeting, Teclistamab, a Bi-Specific Antibody (BSA) was approved by the European Medical Association (like the FDA, but then each country negotiates price and distribution). To everyone’s memory, this is the first time that EMA approved a drug before the FDA. However, in the 50’s EMA did approve Thalidomide for morning sickness for pregnant women, whereas fortunately the FDA never approved (until 2000’s for Myeloma).
- 2) The IMS plans to develop an app called T-MAP which will provides regional therapy recommendations based on that country’s access to treatments.
- 3) Dr Shaji Kumar: “Along with the bone marrow biopsy/aspirate, patients hate 24-hr urine collections the most.”
- 4) Dr S Kumar: “Why do we fail High-risk patients?”
- 5) Dr Paul Richardson (reflecting on Determination trial): “We’re reporting up front study results after 10 years whereas 10 yrs ago, those studies reported after 5 years [reflecting better treatment responses and longer Progression Free Survival (PFS)].”
- 6) Dr Maria V Mateos: “The greatest unmet need is curability.”
- 7) Dr Thierry Facon: “Good discontinuation studies need to be done.”

- 8) There was a 90-minute session on “What it takes to Cure Myeloma?” Cure Definition: No evidence of Disease -> No longer on Therapy -> Limited or no comorbidities from disease -> Mortality similar to age-matched population. Possible answers: Early intervention; better utilization of immunotherapy.
- 9) Dr Peter Voorhees: “We have the tools for a cure; we just need to know how to use them.”
- 10) Dr Sagar Lonial: “I think the Myeloma disease is never more sensitive than at diagnosis.”

Disease Monitoring

- 11) PET-CT can be positive while MRD can be negative, and vica-versa, so the best prognosis is when both are negative. DWI (Diffuse Weighted Image is more sensitive than PET-CT. J Hillengass
- 12) After a CAR-T, MRD+ at 1 month is a poor prognosis, while CR & MRD- at month 12 is required to predict longer PFS. B Paiva
- 13) In MRD- pts, predictors of unsustained negativity include Amp1q, High CTC (circulating tumor cells), and multiple HRCA (High Risk Cytogenetic Abnormalities). M D’Agostino

Disparities in Treatment and Care (GSK sponsored)

- 14) MM women live longer than men. Better lifestyle, lower comorbidities? Black patients are less likely to have High Risk factors. R Popat

Myeloma Clinical Challenges

- 15) Pre-hab exercise -> SCT -> Re-hab exercise result in better physical QoL after SCT. O McCord
- 16) (From MMRD CoMMpass): KCd + maintenance showed better responses in patients without mutations in 5 genes (MGAM, CCDC168, PDXDC1, ABCC1, S1PR2). I Walker

High-Risk (HR) Myeloma (NDMM and RRMM)

- 17) OS for HRMM < 5 yrs and OS for “ultra” HRMM < 3 yrs (Ultra means greater than 1 HR factor). H Avet-Loiseau
- 18) HR questions: a) FISH cutoff for 17p (55%)? b) Keep tp53 (yes)? c) Keep t(14;16)? d) Understanding 1p del? e) FISH vs NGS? f) Clarify impact of multi (ultra) hit? H Avet-Loiseau
- 19) IFM 2018-04: DKRd (x6 cycles) induction for transplant-eligible HRMM (HR = 17p-, t(14;16), or t(4; 14)). For N=50 (68% ultra HR), ORR=96% (>= VGPR 92%); 18mo

PFS = 83%; NGS 10^{-5} =62%. These patients are still to get tandem SCT, consolidation, and Rd 2yr maintenance. C Touzeau

Discovering Targets

- 20) High APOBECs correlates to poorer outcomes. F Kuchenbauer
- 21) MM cells are glutamine-addictive and glutamine metabolism could be a new marker and diagnostic tool for bone disease in MM patients. N Giuliani

Induction for NDMM

- 22) ATLAS: KRd vs R maintenance after SCT. N=178; mPFS 59 vs 41 mos; MRD- 10^{-5} 44 vs 27%. “Risk-adaptive” If KRd results in MRD- after 6 cycles, then R-only maintenance. A Jakubwiak
- 23) DETERMINATION: After 76 mos of follow-up, RVd +/- SCT and R maintenance till progression. N=710 (20% High Risk). Overall mPFS 68 vs 46 mos (SR 82 vs 53; HR 56 vs 17). P Richardson
- 24) GRIFFIN: Final Analysis of RVd +/- Dara (4 cycles) -> SCT -> RVd +/- Dara (2 cycles) -> 2 yr maint R +/- Dara; mFollow-Up 50 mos and all pts completed \geq 1 year after end of study. N=207, Dara arm showed benefit in ORR (83 vs 64%), CR (67 vs 48%), MRD- 10^{-5} (64 vs 30%), MRD- \geq 1 yr (44 vs 14%), and 4 yr PFS (87 vs 70%). No difference in 4 yr OS (both 93%). mPFS and mOS not yet reached. Side effects similar in each arm. D Sborov.

What does it take to Cure Myeloma? (Janssen sponsored)

- 25) When can we consider a patient cured? Dr. S. Jagganath “MRD- for 5 years.” Dr T. Martin “But not treatment for 5 years.” Dr S. Giralt “Need RCT’s (Randomized Clinical Trials)”.

Relapsed MM

- 26) ICARIA: IsaPd vs Pd. OS benefit of 7 mos. Prior Dara -> Isa...not successful; prior Dara -> IPd...some success but better to have an interim treatment. P Richardson
- 27) IKEMA: Kd +/- Isatuximab. CR = 44 vs 29%; MRD- 10^{-5} = 26 vs 12%. R Hajek
- 28) Baseline ocular conditions such as cataracts, glaucoma, or blepharitis (eyelid inflammation) do not affect Blenrep ocular symptoms. R Popat
- 29) Managing Rev-refractory patients: DPd, DKd, IsaKd. N Bahlis

- 30) AMaRC: BelaKd for previous LOT 1-3, and being refractory to prior PI (K, V or I) was allowed. Blenrep was only given every other cycle (e.g every 8 weeks). For N=10, half pts had blurred vision (2 Gr ≥ 3) and 7 had decrease of ≥ 3 lines in Snellen eye chart ("E") considered Gr 3, however most patients improve with dose-holding. ORR was 9 of 10 pts (8 at least VGPR). Amending protocol to lower Blenrep from 2.5 mg/Kg down to 1.9, 1.4, or 1.0. Early results so most effective dosing is still being determined. H Quach

Immune Reconstitution and Vaccination

- 31) Being on CD38 or BCMA treatments causes Covid vaccines to be less effective producing antibodies. E Terpos
- 32) On average, Bi-specifics cause 50% infection rates, and 25% grade 3 or 4. H Ludwig

Integrating Immunotherapy into MM Treatment Landscape (BMS sponsored)

- 33) Ways to possibly overcome resistance in CAR-T: GPRC5D CAR-T rescue mice that are BCMA deficient. Dual BCMA/GPRC5D CAR-T. Gamma Secretase Inhibitors, which increase BCMA. E Smith
- 34) Cereblon in MM cells is a target of IMiDs but Cereblon is also found in T-cells and NK-cells, explaining IMiD activation of the immune system. S Trudel

Cellular Therapy

- 35) CARTITUDE-2 Cohort A 1-3 previous LOT. N=20, mFU 17 mos, 40% triple refractory. ORR 95% (CR 90%, rest VGPR), mPFS 75%, mDOR NR but estimate 90% will be in response at 1 yr. MRD- 10^{-5} 100%, ICANS/neurotoxicity 30% (1 Gr 3). Parkinsonism decreased from 6% in CARTITUDE-1 to $<0.5\%$ after implementation of patient mgmt. strategies. A Cohen
- 36) CARTITUDE-2 Cohort B early relapse after initial therapy (< 12 mos non-SCT pts, or within 12 mos after SCT). N=19, mFU=13 mos, 80% SCT, ORR 100% (95% \geq VGPR) MRD- 10^{-5} 14 of 15 pts, MRD- 10^{-6} 8 of 13 pts. 1 yr PFS 90% (!). N van de Donk
- 37) Teclistamab (N=165) vs Real World Physician's Choice (N=248) with similar characteristics, e.g ≥ 3 LOT, triple class refractory, ISS stage, etc. Tec arm much better as seen in ORR (63 vs 27%), DoR (18 vs 5 mos), mPFS (11 vs 4 mos), mOS (18 vs 14 mos). [Side note: Teclistimab is widely expected to gain FDA approval soon, the first USA bi-specific.] N van de Donk
- 38) Efficacy of Cilta-cel (Carvkti) in patients with progressive MM after prior BCMA ADC Blenrep. N=13, ORR 62% (all \geq VGPR), mPFS 9.5 mos, DoR 11.5 mos. A Cohen

- 39) Efficacy of Cilta-cel (Carvkti) in patients with progressive MM after prior BCMA bi-specifics. N=7 with mLOT=8(!), ORR 57%, mPFS 5.3 mos, DoR 8.2 mos. J San-Miguel
- 40) QoL after CAR-T: Most patients back to baseline QoL and even better but some issues persist 3 or 6 mos later: Pain & fatigue, financial toxicity. S Sidana
- 41) Efficacy/safety of CAR-T in elderly pts (≥ 70 yo). N=19 (compared with N=58 younger pts). Safety/toxicity no difference. ORR 84% vs 90%. MRD- 10^{-5} the same, as was PFS. However, OS was a bit better for elderly. K Reyes

Other

- 42) Celmod Mezigdomide (“Mezi”) in combinations MVd and MKd for RRMM. One-third required dose reductions so Mezi 1.0 mg final dose (14 days on, m 7 off). 60-80% ORR for N=86. Some infections. P Richardson
- 43) Bi-specific RENG5458 (BCMAxCD3) for N=73 RRMM with mLOT=5 and 89% triple refractory. Among those responding 86% \geq VGPR, 43% CR. At 200-800mg, 75% ORR (N=18 of 24). CRS 38% (no grade 3 or 4). Fatigue 45% (all but 2 were grade 1 or 2). N Bumma
- 44) Assessment of salvage therapies (median=3) after BCMA CAR-T (presented by 2nd yr med student at UCSF). Subsequent treatment ORR results [N=42, %ORR]: BCMA CAR-T [N=8, 75%], BCMA BsAb [N=5, 60%], BlenRep [N=7, 29%], Anti CD38 [N=19, 53%], Alkylator [N=41, 46%], PI [N=32, 41%], IMiD [N=16, 38%], Selinexor [N=8, 38%], Venetoclax [N=6, 33%], Elotuzumab [N=4, 25%]. mOS=15 mos. K Reyes
- 45) MMRF’s MyDRUG “umbrella” trial: N=16 RRMM (early relapse) with N/K-RAS or BRAF mutations given Cobimetinib + dex, (2 cycles) then Cobimetinib + IPd. ORR 47%. S Kumar
- 46) Ph 1 study of a bi-specific ABBV-383 (BCMA x CD3) for RRMM, mLOT=5, no step-up, every 3 week dosing. N=60, 41% infections (24% Gr3/4), 72% CRS (N=1 Gr 3/4), ORR 60% (\geq VGPR 43%) at 60mg dose, MRD- 10^{-5} 8 of 11 pts, mPFS 10 mos for whole population but not reached for 60mg dose although expect 1 yr PFS 58 mos. P Voorhees

SUMMARY

In my 27th year of myeloma diagnosis, it never ceases to amaze me the amount of progress MM treatments make every year. In addition, more is known about the myeloma cell biology, microenvironment, and immune system, so more studies are focused on finding new treatment targets. In addition, dosage adjustments, patient long-term outcomes, sequencing therapies, which drug might work best for which patient, and “cure” discussions are all getting more attention than ever before.