MYELOMA HIGHLIGHTS FROM ASH CONFERENCE "VIRTUALLY" 12/8-12/2023

According to Jack Aiello (definitely not medically trained)

PREFACE

This is my 18th year attending the 66th annual ASH (American Society of Hematology), where typically over 30,000 attendees from all over the world (hematologists/oncologists, lab researchers, oncology nurses, scientists & 300 pharma companies) attend. There is no other single conference where so much information is presented about Multiple Myeloma (MM). This year ASH was set up as a hybrid meeting where about 2800 attended in person and 4000, including myself, virtually. That said, I watched many of the presentations as they were happening, asked a few questions that were answered in real time, and watched replays of other talks. There were more than 800 myeloma-related abstracts, with about 100 selected for oral presentation. I'm grateful to the IMF (www.myeloma.org) and their sponsoring pharma donors BMS, Janssen, Karyopharm, Regeneron, and Takeda for registering me for ASH so that I could learn and subsequently share my patient perspective with you.

As background, I attended my first ASH meeting 18 years ago and found it a bit like being diagnosed with myeloma 29 years ago. The terminology and amount of information was overwhelming. Rather than attending talks on Biology, I typically focus on the Clinical Trials, which I'm able to understand and are more relevant near-term to patients. One advantage of the virtual experience is that I could replay presentations that I either missed or wanted to be clear on details after having viewed the printed abstracts in November. You might want to view the published abstracts as well at www.hematology.org and various press releases. Wherever possible, I've listed Lead Investigator and Abstract# after the trial results, e.g. [Chari, 1010]. Searching on the abstract number will take you to the actual abstract for a limited amount of time. Note though that the data results presented is often updated from the on-line abstract.

There are other ways to learn more about results from this conference. I know the various myeloma advocacy organization will have webinars of ASH highlights. The IMF (www.myeloma.org) had a Facebook live event, replace now available; their IMGW Conference Series on 12/14…replay coming, and Top Myeloma Research webinar featuring Dr Durie and 2 patients on Jan 4. You'll also find some patient blogs (including mine) on the IMF website (https://ash2023blogs.myeloma.org/). And all of us in the SF Bay Area should attend the in-person-only LLS Blood Cancer Conference (which includes updates from ASH) Saturday Feb 3, 2023 (register at https://na.eventscloud.com/website/63661/). Dr. Ajai Chari from UCSF, who presented ASH in person, will do a great job presenting the latest information.

Even virtually, presentations of clinical trial results followed the same format: Background (including hypothesis), Study Objective, Design & Treatment schema, Patient Characteristics & Cohorts, Responses (include high-risk cytogenetics), Toxicity (hematological and non-hematological), and Conclusion. Remember, the goal of Phase I (typically handful of patients) is to determine "Maximum Tolerated Dose" and/or Recommended Ph2 Dose (RP2D); Phase I/II and II (typically 25-75 pts) continue to measure dosage escalation and safety while looking at responses; and finally Phase III (several hundred patients) compares response rates between new and current standard of care (SOC) treatments.

Treatment schemas are defined for stages of **Induction**, and optionally **Transplant (SCT)**, **Consolidation**, and **Maintenance** with specified **Randomization** along the way for newly diagnosed pts (**NDMM**) relapsed/refractory pts (**RRMM**). Dosage amounts and scheduling are provided for each

drug along with optimum number of treatment cycles (typically 28 days). **Risk stratification for MM** is determined by cytogenetics-FISH analysis (e.g. chromosome deletions and translocations) and gene-expression profiling (GEP). And while all these details are provided in the actual abstract, I don't necessarily list them below.

HIGHLIGHTS (e.g. My Takeaways)

1. This year's ASH continued to expand our knowledge on immunotherapies…more CAR-T's and bispecific antibodies ("T-cell directing therapies") as well as more targets besides BCMA…and most importantly, side effects such as cytopenia (lower blood counts), cytokine release syndrome (CRS), neurotoxicity, and infections.

2. How does real-world experience of recently approved drugs compare with their clinical trial that let to FDA approval? This report has a section dedicated to real world studies.

3. 4-drug induction before transplant is here to stay.

4. Diversity, Equity and Inclusion (DEI) was discussed more at this ASH than ever before although this year I did not attend or report on most of these talks.

COMMENTS AND DISCUSSIONS I FOUND PROVOCATIVE

5. O Nadeem: "Mortality clearly correlates to drug access."

6. O Nadeem: "Blacks have a higher prevalence of MGUS than white (4% v 2%) and are 5 years younger when diagnosed with MM."

7. C Cole: "Being poor will kill you with disease."

8. C Cole: "In CT's, broaden eligibility criteria, eg lower ANC to recognize Duffy noll syndrome, and incorporate a diversity inclusion plan."

9. C Cole: "Blacks have higher t(11;14) but lower del17p."

10. O Landgren: "Over 40 combinations are listed in NCCN Guideines."

11. O Langren: "I feel some patients diagnosed in '23 and '24 will have the same lifespan as the general population."

12. N Joseph: "SMM is defined as BMPC" >= 10% and/or m-spike >= 3 g/dL, no symptoms."

13. N Joseph: "3yr PFS of 89% for the ASCENT trial ("curative treatment") was the same as Rev-only trial."

14. N Joseph: "For my patients diagnosed with HR SMM, I first talk about available clinical trials and then suggest Rev-only."

15. O Langren: "15%-35% of patients are lost at the end of each LOT (Line of Treatment)."

16. N Joseph: "Around 6 months I taper my patients off Dex." J Mikhael "#downwithhdex"

17. L Costa: "BCMA occurs on all plasma cells, even the good ones."

18. L Costa: "Abecma v Carvykti: Onset of CRS is 1 day vs 7 days."

19. F Maura discussed CAR-T/Bispecific relapse due to antigen loss. While he said this is true for GPRC5D, this is not the case for BCMA. Relapse on BCMA treatment is due, in part, other antigens escaping and blocking treatment binding. A second cause is high levels of soluble BCMA (found in serum) which alters CAR-T activity.

20. R Orlowski: "For a standard patient who achieve CR from induction, and especially MRD, I encourage the patient to harvest stem cells but am ok with them not going ahead with a transplant."

21. S Lonial: "Rumors of the demise of transplants is greatly exaggerated."

22. R Orlowski: "Isatuximab may have better activity in 1Q+ patients than daratumumab."

23. N Raje: "Like many MM drugs, they often get approved and then we figure out how to use them. This is the case with Blenrep."

24. P Richardson: "Selinexor + Venetoclax for t(11;14) pts is possible as long as supportive care (e.g. short term follow-up visits) is available.

25. S Lonial: "With CD38 mAB's, we need to be more conscious of infections."

26. S Lonial: "A wearable bolus injector disc (looks like the end of a stethoscope) is used for subQ Isatuximab injection over 3-5 minutes."

27. A Krishnan: "CAR-T waiting time has come down from 5 months last year to 2-3 mos today."

28. N Raje: "Cartitude-6 study comparing CAR-T vs SCT includes 2 yrs Revlimid maintenance in both arms."

29. S Lonial: "BCMA BsAb and CAR-T infections is profound because plasma cells are being wiped out."

30. A Krishnan: "The neuropathy signal is real with BsAb Elranatamab."

31. P Richardson: "Celmods do not appear to have the same secondary primary malignancy risk as IMID. Also very few G3/4 side effects."

MGUS & SMOLDERING MM (early screening)

32. Immuno-PRISM: A small study (N=19, 12 evaluable) where Teclistamab is given to HR-SMM (2-3 factors using 20-2-20) pts. CR for 10 of 12, VGPR for other 2. 100% MRD- at 10^{-6}. Longer terms results will be interesting. [Nadeem, 206]

33. This study examined low risk SMM pts (M-protein <2g/dL and Free Light Ratio <20). Their results showed that pts with an evolving MP (>=0.4g/dL) and eFLR (>= 40 increase) was associated with a median time to progression of 25 mos, the same as high risk patients at baseline. [Akhlaghi, 877]

34. For N=54 HR SMM pts, this effective treatment of KRd (8 cycles) followed by Rev maintenance (2 years) showed sustained MRD negativity. With a media follow-up of 5 years, 93% of patients show no progression and 40% are MRD- (10^{-5}) for at least 2 years. [Hill, 337]

FRONTLINE (INDUCTION OR FIRST LINE) THERAPY TRANSPLANT-Eligible

35. This study looked a newly diagnosed HR MM pts (N=50) who received DKRd induction followed by a tandem SCT plus consolidation (on between transplants as well as after the 2nd one) followed by 2 yrs Dara-Rev maintenance. This is an aggressive treatment for patients and resulted in 42% discontinuation. Efficacy results showed 94% MRD- (10^{-6}), 30mo PFS = 80% and 30mo OS=91%. [Touzeau, 207]

36. When your abstract is selected to be presented within the plenary session, it's denoted as one of the top abstracts at ASH. Such was the case with Dr Francesca Gay's abstract: This Ph3 IsKia trial comparing Isa-KRd vs KRd as induction and post-SCT consolidation (x4) and "light" consolidation (x12). The Primary Endpoint was MRD (not yet approved as a surrogate for PFS or OS). After consolidation, MRD- at 10^{-5} was 77% v 67% and at 10^{-6} 67% v 48%. For very high risk pts (2 of more high risk factors), MRD- at 10^{-6} was 77% v 27%. Although MRD improved at every phase, ORR of 94% was essentially the same for both arms. Dr Gay plans to provide 1-year MRD sustainability in 2024 but this, along with another abstract presented this coming Tuesday, really strengthens the benefits of 4-drugs v 3. [Gay, 4]

37. The Emory 1000 refers to patients at Emory initially treated with RVd and then subsequently with Dara-RVD when the Griffin showed 4-drug benefit. This particular study compares these 2 regimens (including SCT, maintenance) for both standard and high-risk NDMM pts. For std-risk pts, 2-yr PFS for D-RVd vs RVd is 94% vs 84% and for high risk 83% vs 69%. The 2-yr OS for the same groupings is 96% vs 93% and 94% vs 79%. [Joseph, 647]

38. Perseus is a phase 3 study of Dara+RVd vs RVd followed by SCT, consolidation, and maintenance (DR or R, and MRD- after 12 mos, Dara was deleted. This was put on by the EMN (European Myeloma Network), 130 institutions, and 11 countries (including Australia). For N=709, the Dara arm exceeded the non-Dara arm in every measure: 4yr mPFS: 84% v 68%; CR 88% v 70%; MRD- (10^{-6}) 65% v 32%. And 64% of the Dara maintenance arm was able to stop the Dara although I don't know the relapse rate. (It's pretty clear that between this and the Plenary talk, the 4-drug regimen is here to stay for Transplant-eligible patients…that is until CAR-T's take over.) [Sonneveld, Late Breaking Abstract-1]

CAR-T STUDIES, ALL PTS RRMM, ALL TARGETING BCMA UNLESS OTHERWISE NOTED

39. Health-Related Quality of Life (HRQoL) analysis of the large KarMa 3 study which randomize patients into Abecma arm (N=254) or Standard of Care arm (N=132). Using several Patient Reported Outcomes (PRO's) studies, fatigue, pain, physical and cognitive functioning were all better in the CAR-T arm. [Delforge, 96]

40. This presentation actually discussed the development of a CAR-T to increase persistence and long-term efficacy. Out of this came 2 CAR-T's: a) BCMA D8 Fab CAR and 2) a dual targeting BCMA and CD19 AUTO8 CAR. They are tested against each other in the MCARTY study, which is still recruiting for Phase 1 (11 pts have in induced so far). At a median follow up of 6 mos, there were no reported cases of ICANs, no grade 3/4 CRS, 100% ORR with 2 cases of ongoing sCR>12 mos. Something to watch. [Lee, 350]

41. Eque-cel, another BCMA CAR-T from China, showed good results in a Phase 2 trial (FUNMANBA-1) for N=88 pts, with 3 or more prior LOTs. The focus of this study was on outcomes and characteristics of pts who achieved sustained MRD- (10^{-5}). Overall 94% achieved MRD- and 81% had sustain MRD- for >= 12 mos. Factors that impacted sustained MRD were High Risk, BCMA expression, and bridging therapy. There was only a weak correlation between persistence and MRD- duration. [Li, 761]

42. We now have longer study results for Cartitude-2 CAR-T trial with a follow-up of 29 mos, Cohort A N=20 Rev-refractory 1-3 LOTs and Cohort B N=19 1 prior LOT. Originally reporting 95% and 100% ORR for the 2 groups, MRD- at 10^{-5} shows 100% and 93% respectively. And sustained MRD >12 mos was 52% and 62% respectively. Finally 2 yr PFS was 75% and 73% while 2 yr OS was 75% and 84%. Neutropenia Grade 3/4 was about 95% and 90%. [Hillengass, 1021]

43. Updated results were also provided for GC012F FasTCAR-T (24 hr production) targeting BCMA and CD-19 for N-22 first line NDMM pts. They achieved 100% ORR and CR as well as 100% MRD- at 10^{-6}. No grade 3/4 CRS or ICANS. [Lu, 1022.]

44. Another new CAR-T study was presented CART-Ddbcma for N=38 for RRMM with >=3 LOTs. The "Dd" apparently stands for "domain" reflecting a more stable binding. With 1 yr of follow-up, ORR=100% (>=VGPR 92%), and 2yr PFS of 56%. MRD at 10^{-5} was 89%. Importantly, the efficacy rates were similar for HR pts. As a Phase 2 trial, this will come from Kite Pharma and be called iMMagine-1, now enrolling. [Frigault, 1023]

45. And we have yet another new BCMA CAR-T ARI0002h that included a booster dose at day 100 for N=60, >=2 LOTs but no prior BCMA. ORR% was 95% within first 3 mos and MRD at 10^{-6} on days 28 and 100 were 98% and 96% respectively. Estimated mPFS was 16 mos which was also the case for HRMM. [Oliver-Caldes, 1026]

46. This CAR-T study focus on patients with extramedullary (tumors separated from the bone) and paramedullary (tumors attached to the bone) disease. It compared N=134 pts, 75 with neither, 34 with EMD, and 25 with PMD. It turns out that the presence of EMD but not PMD was associated

with significantly worse PFS and OS. For example, mPFS was 24mos, 12 mos, and 26 mos respectively. And the OS risk was 4 times as great. [Pan, 1006]

47. BMS-986393 is a GPRC5D CAR-T about to enter ph 2 with a dosage of 150M reengineered t-cells. Overall results from ph 1 with varying dosages for N=84 pts (including 41% High Risk, 46% prior BCMA) 88% ORR as well as 83% ORR for HR pts. At the RP2D with N=26, ORR was 91% (CR 48%) and infections were relatively low at 35% and 12% for grades 3/4. [Bal, 219]

BISPECIFICS (myeloma cell X t-cell)

48. This poster updates Phase 1 results for Alnuctamab, a BCMAxCD3 bispecific from BMS. For N=73 (44 pts at 30mg or >30mg) subQ ALNUC appears safe with a low rate of severe infections 62%/16% of pts. Across doses, responses were durable and deepened over time, with 100% of CR responders achieving MRD negativity (10^{-5}). High antitumor activity was observed at target doses ≥ 30 mg (ORR 63%) and specifically at the 30-mg target dose (ORR 69%). [Bar, 2011]

49. JNJ-5322 is a trispecific targeting both BCMA and GPRC5D on the MM cell. It's only been studied in patient samples so far and is starting a phase 1 trial, but I decided to include in this report due to its relative uniqueness. [Pillarisetti, 456]

50. In an Education Program, Dr Surbhi Sidana (Stanford) review toxicities associated with BiSpecifics. If CRS is experienced, she encouraged the use of Tocilizomab, which itself does not add to other side effects. If ICANS (neurotoxicity) is experienced (20% CAR-T, 5-10% BsAb's) both steroids and Anikinra are effective. About 3-4 weeks out, about 6% of Abecma pts experience Parkinsonism (don't really know how to treat…maybe steroids, cytoxin?); and 6% of Carvykti pts experience Bells Palsy (facial droop) which tends to resolve itself. Finally, both CAR-T BsAb's cause high rates of Cytopenias (blood count reductions) and Infections, except lower rates in GPRC5D cell therapy. Expect to take prophylactics for infection and IVIG. GPRC5D also causes side effects to skin (both rash, non-rash), nails, and dysgeusia (loss of or altered taste).

51. Dr Chari (UCSF) presented efficacy and safety results of lower Talquetamab dosing. Today the approved recommended dose is .4 weekly or .8 every other week. Side effects from this MonumenTAL-1 study included dysgeusia=77%, skin (such as peeling)=73%, nail=63%, and skin (rash)=40%. Interestingly, these side effects were not seen when Talq was being tested at lower doses. N=25 dose-reduced to .4 every 2 weeks or N=10 dose-reduced to .8 every 4 weeks. Responses compared favorably versus original dosing: ORR (79 v 72%); 12mos PFS (50 v 54%). And side effects decreased across the board, and no new side effects. This might be a perfect example that dosages should be selected by MED (Maximal Effective Dose) rather than MTD (Maximal Tolerated Dose). More isn't always better! [Chari, 1010]

52. HPN217 is a *tri*-specific, targeting CD3 on the T-cell and both BCMA and Albumen on the MM cell, the latter for increased half-life extension (longer persistence). In this phase 1 trial for N=97 R/RMM pts, 12 mg dose resulted in ORR=63% so will be the recommended Phase 2 dose. [Madan, 1012]

53. First results of the Phase 1b MonumenTAL-2 study were shown. Talquetamab + Pomalidomide were given to N=35 RRMM pts. As was shown earlier Talq is either given weekly (QW) or every

other week (Q2W). ORR was 94% and 84%, >=CR was 63% and 37%, and >=VGPR was 88% and 69% respectively. There were 23% grade 3/4 infections. [Matous, 1014]

REAL WORLD COMPARISONS

54. After consolidating 8 trials in Canada, the conclusion was that the corresponding clinical trials showed mPFS 3-18mos higher and mOS >19 mos more than real world patients. As such RW pts are experiencing 44% worse PFS and 75% worse OS compared to randomized clinical trial patients. [Visram, 541]

55. This study examined N=110 pts across multiple institutions and compared these real-world results with MajesTEC-1 study that resulted in FDA approval of Teclistamab. MajesTEC-1 reported ORR=63% and mPFS=12mos. In contrast, the real world study, which included both triple class and penta-refractory, as well as prior BCMA (not allowed in MajesTEC-1) patients, ORR=62% (very similar) and 6-mos PFS=52% (so likely worse). Use of prophylactics such as IVIG improved infection rates. [Mohan, 545]

56. Dr Sidana (Stanford) showed real-world results for Ide-cel using the CIBMTR database with 821 RRMM pts, three-fourths of whom would have been ineligible for the Ide-cel trial. Overall, both efficacy and ASE results were very similar to the KarMMa trial. ORR was 78%, mPFS was 9 mos and 1yr OS est=67%. It should be noted that prior use of BCMA (ADC or BsAb) resulted in lower PFS and OS by a few months. [Sidana, 1027]

57. This abstract examined "real-world" safety and efficacy of Teclistamab. You'll see the term "real-world" used to mean patient results after FDA approval who are taking the treatment commercially approved. In fact, many of these patients (83% in this case) would have not qualified to be in the registration trial (MajesTEC-1) that resulted in Teclistamab's approval. For N=106 pts, ORR was 66% (ORR for MajesTEC-1 was 63%]. Further ORR's for prior BCMA usage were 50%, 57%, 80%, and 33% for patients who had an ADC, CAR-T, ADC + CAR-T, or ADC+other respectively. [Dima, 91]

OTHER Drugs

58. For N=120 (40 per dosage cohort), Iberdomide (an oral Celmod) may well be an effective maintenance treatment following an SCT. During the first 6 cycles of maintenance, at the 1.3mg dose, CR improved from 28% to 53%. At the 1.0mg dose, CR increased from 25 to 40%. [van de Donk, 208]

59. Venetoclax, approved for lymphoma but not yet for Myeloma (so available off-label), continues to show good results for t(11;14) RRMM pts. For N=55 pts in the Ven-Dara-dex (VenDd) arm vs N-26 in the Dara-Vel-dex (DVd), VenDd showed superior ORR (96% v 65%) and mPFS (46 v 15mo). MRD negativity at 10^{-5} and 10^{-6} respectively were 40 v 24% and 24 v 6%. [Bahlis, 338]

60. Blenrep + Kd was given in a Ph I/II N=65 RRMM pts. Blenrep was only given once every 2 mos. Treatment-related AEs were reported in 93% of pts (Gr3 60%, Gr4 13%), including blurred vision (40%, 7.3%, 0%). Ocular AEs occurred in 42 (79.2%) out of 53 evaluable pts including decline in best corrected visual acuity (BCVA) (total 77.2%, Gr1 9.4%, Gr2 33.9%, Gr3 33.9%) and keratopathy (K) (total 75.4%, Gr1 5.6%, Gr2 22.6%, Gr3 47.2%). The preliminary efficacy data is encouraging with deep

responses observed after only 2 cycles of therapy. ORR and ≥ VGPR by end of cycle 2 were 80% and 40% respectively. [Lasica, 2012]

61. I mention this study because it's the first trial result to come out of the Asian Myeloma Network (AMN) established in 2011 by the IMF. Today it consists of 10 countries and 160 members. They compared PCd vs Pd for N=122 RRMM pts with a mLOT = 3. The results were that PCd improved mPFS (11 v 6mos), ORR (61 v 38%) and Duration of Response. [Chng, 1009]

62. Sonrotoclax is a next generation Venetoclax inhibiting BCL2 with a potency >10x. Sonrotoclax 640mg plus dex was given to N=10 R/RMM pts harboring t(11;14). ORR was 70% (7 of 10) for this small group of patients. lQuach, 1011]

63. Mezigdomide (a Celmod, known as Mezi) plus dex plus either Dara or Elo were compared. For RRMM pts with 2-4 prior LOT's. For N=79 on varying dosages of Mezi, the MeziDd and MeziEd ORR's were 75% (although one of the doses was 89%) and 45% respectively. However grade 3/4 AE's MeziRd and MeziEd were 77% and 95% respectively, with neutropenia and infection having the highest impact. [Richardson, 1013]

64. Here's a very interesting study that examines dex dose reduction in the large SWOG trials S0777 and S1211 which both had pts using dex at the 40mg dosage. However, more than half the patients dose-reduced without changing their PFS and OS outcomes. Perhaps 40mg of dex is not needed for the entire length of induction. [Banerjee, 1066]

65. We know that infection rates are high with immunotherapy treatments. This study looked at RRMM pts treated with either anti BCMA (N=200) or anti GPRC5D (N=29) bispecifics. Overall infection types are bacterial (56%), viral (38%), fungal (5%) and parasitic (1%). BCMA v GPRC5D infection rates were 73 v 53%. To reduce infection rates, minimize steroid use and space out injections. [Cellerin, 1005]

OTHER RESULTS

66. How do you treat a "functional" High Risk patient, which is commonly defined as a patient who doesn't necessarily show High Risk cytogenetics but rather shows suboptimal response (< PR) or relapses shortly (< 18mos) after induction? Dr F Gay suggested considering KRd, or the addition of Dara (if it wasn't part of induction), or CAR-T's which are expected to be available for earlier lines of treatment based on recent trial results. [Gay, Education Program]

67. Dr M Hartley Brown tackled the question of relapsed after induction that including and anti-CD38 treatment (Dara or Isa). She reminded us not to forget about a transplant if it wasn't part of the first line. Selinexor as well as BCMA-targeted therapies should also be considered (which includes Blenrep which hopefully once again receives FDA approval). [Brown, Education Program]

68. Finally, Dr A Cohen considered treatment options after a patient relapses from BCMA treatment. Another BCMA treatment could be considered (although not the same as previously tried). A non-BCMA treatment might be preferred. Or even a non-T cell-directed therapy might be tried. [Cohen, Education Program]

69. Higher fibrinogen and ferriten values assessed at baseline were associated with inferior OS after CAR-T. Higher baseline ALC was also associated with high risk of ICANS and higher grade ICANS. Perhaps these biomarkers will be incorporated in assessing risk of CAR-T therapy. [Pan, 92]

SUMMARY

This year's ASH continued to amaze me with so many studies in Myeloma, focusing on all stages from Smoldering Myeloma to MM Induction through Relapse. Clearly immunotherapy treatments, CAR-T's and Bi-specific T-cell engagers were predominant among the oral presentations I attended, providing longer-term data on these new treatments. And importantly, other targets besides BCMA are being investigated.

At the IMF public facebook event at the end of ASH, I asked Dr Joe Mikhael "When will we have personalized medicine for MM pts. His answer concluded that we're already there in this respect. When he sees a patient, he studies the patient's myeloma, past treatments, treatment responses, comorbidities, and goals/desires. Only after that is it appropriate to discuss and consider a treatment option. And with 19 FDA approved MM treatments in the last 20 years, and many more combination therapies as well as so many trials, we have a better chance than ever before of providing the patient with an excellent treatment.

For someone diagnosed with stage III MM 29 years ago with only 2 treatment options available (MP or VAD-SCT) and given 2-3 years expected survival, I've seen incredible progress since 2003 when Velcade was first approved followed by 18 more approvals and many combination therapies. While there continues to be unanswered questions, we now have many more effective treatments for MM, providing patients with better opportunities to manage their disease. NDMM patients can justifiably be more optimistic about their new diagnosis than at any other time in history. ASH2023 highlighted the tremendous advances we have made in treating this cancer for both the newly diagnosed and relapsed patient. That said, most patients still relapse so being educated about your myeloma, looking down the road at next possible treatments, and knowing what question to ask your doctor continue to be the best medicine.

Be your own best patient advocate.

GLOSSARY (according to Jack)

Drug (brand names) by Drug Class/Category

IMID – Immunomodulary Drug
T – Thalidomide
R – (Lenalidomide) Revlimid
Pom – Pomalidomide (Pomalyst)

PI – Proteasome Inhibitor
V- Velcade (Bortezomib)
Cfz, K – Carfilzomib (Kyprolis)
I, Ixa – Ixazomib (Ninlaro)

mAb – Monocloncal Antibody
D, Dara – Daratumumab (Darzalex)
E, Elo – Elotuzumab (Empliciti)
Isa – Isatuximab

HDAC - histone deacetylase inhibitors
Pano – Panobinostat (Farydak) but no longer FDA approved in the US

Steroids
P – Prednisone
D or d - Dexamethasone

Chemotherapy Drugs
C – Cyclophosphamide (Cytoxan)
M – Melphalan

Treatment Measurements
EFS – Event-free Survival
ORR – Overall response (>=PR)
OS – Overall Survival
PD – Progressive Disease
PFS – Progression-free Survival
PFS2 – PFS + next-line treatment PFS
TTP - Time to Progression
TTR - Time to Respond

Treatment Response
CR – Complete Response: No sign of MM (0 M-spike)
nCR – Near CR (positive M-spike, may be same as VGPR)
MR – Marginal Response: 0-50% reduction in MM
PR- Partial Response: 50% reduction in MM
SD – Stable Disease i.e. no response but also not worse
sCR-Stringent CR: CR+ normal FLC & no clonal cells
VGPR – 90% reduction in MM
MRD – Minimum Residual Disease typically by Flow Cytometry (NGF) or DNA sequencing (NGS) to provide more sensitive measure of MM (e.g. 10^{-5} or 10^{-6})

Side Effects
AE (ASE) – Adverse Event (Adverse Side Effects)
DVT - Deep Vein Thrombosis (blood clots)
MTD – Maximum Tolerated Dose
ONJ – Osteonecrosis of the Jaw
PE – Pulmonary Embolism
PN – Peripheral Neuropathy
QOL – Quality Of Life
VTE - Venous Thromboembolism (PE + DVT)
CRS – Cytokine Release Syndrome

Tests/When to treat?/Other
CRAB – High Calcium, Renal, Anemia, and Bone…
CRABi – CRAB + "i" increased infections
FLC – Free Light Chain

SCT – Auto stem cell transplant.
TE, NTE – Transplant Eligible of Not TE

LOT – Lines of Therapy

TE, nTE – Transplant eligible or non-TE

"d" and "D" – Typically both mean Low-dose Dex (40 mg/week) these days
MGUS – Monoclonal Gammopathy of Undetermined Significance
SMM – Smoldering MM
Pt(s) – Patient(s)
n - Number of pts
R/R- Relapsed/Refractory, Ref defined progressing while on Tx or within 60 days.
HR – High Risk (For MM: typically t(4;14), t(14;16), t(14;20), Del 17p, Gain/Amp 1q, GEP; For SMM: 20:2:20 means >20% plasma cell, >2 M-spike, >20 FLC ratio
RP2D – Recommended Phase 2 Dosage