

## MYELOMA HIGHLIGHTS FROM ASH CONFERENCE “VIRTUALLY” 12/9-12/2022

According to Jack Aiello (definitely not medically trained)

### PREFACE

This is my 17<sup>th</sup> year attending 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. This year ASH was set up as a hybrid meeting where some attended in person and many, including myself, virtually. That said, I watched most of the presentations as they were happening, asked a few questions that were answered in real time, and watched replays of other talks. Both oral (3 digits) and poster (4 digits) abstracts were presented on all blood diseases, especially cancers. There are typically more than 900 myeloma-related abstracts, with about 100 selected for oral presentation. I'm grateful to the IMF ([www.myeloma.org](http://www.myeloma.org)) and their sponsoring pharma donors Takeda, Amgen, and Karyopharm for registering me for ASH so that I could learn and subsequently share my patient perspective with you.

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](http://www.hematology.org) and various press releases. Wherever possible, I've listed Lead Investigator and Abstract# after the trial results, e.g. A Nooka, 4560]. 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 webinar is 12/20). You'll also find some patient blogs (including mine) on the IMF website (<https://ash2022blogs.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 4, 2022 (register at <https://www.lls.org/article/blood-cancer-conferences>). Dr. Jeff Wolf from UCSF, who attended 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. High Risk MM, ultra-high risk MM, and high risk Smoldering myeloma are all identified as areas where better treatments (and clarifications to treat HR SMM) are needed.
3. MRD (Minimal/Measurable Residual Disease) and Mass Spectrometry are methods for assessing a patient's amount of MM, and certainly more sensitive than the SPEP/IFE blood tests that are used to determine M-spike and response levels. They are good prognosticators but typically not used to help guide treatment (for example, when to stop maintenance). MRD by next generation sequencing or flow requires a bone marrow biopsy whereas mass spec uses blood (but may not be as sensitive).
4. We have many treatments available these days but what's the best treatment for a patient being newly diagnosed, transplant-eligible or not, maintenance (for how long), treatment at first relapse, subsequent relapses? Many of the study results below try to answer these questions via clinical trial results (but that's still not a personalized treatment so it's always important to ask your doctor questions and be part of that shared decision making).
5. Diversity, Equity and Inclusion (DEI) was discussed more at this ASH than ever before and got its own section below.

## **COMMENTS AND DISCUSSIONS I FOUND PROVOCATIVE**

6. "Despite progress with newer therapies, challenges remain in delivering effective treatment to MM patients." Dr N Munhsi
7. "There's more to determining High Risk Smoldering MM (HRSMM) than the 2-20-20 formula, such as speed of disease progression, cytogenetics, and more." Dr J San Miguel
8. "Treatment for HRSMM should be either Rev/Rev-dex or a clinical trial." Dr SV Rajkumar
9. Dr S Kumar said "At Mayo we use 4-drug induction therapy for HRMM but will wait for more evidence before using 4-drugs for Standard Risk MM." Contrarily, Dr T Martin: "At UCSF, we use 4-drugs for everyone."
10. Dr Moreau noted "Perhaps we should be using 2 drugs (Dara-Rev) for maintenance of HRMM pts."
11. "Relapse within 12 mos of an SCT should be considered high risk [even if cytogenetics do not show mutations]." Dr SV Rajkumar
12. "We lose between 15-35% of patients at the next relapse so we always want to give the best treatment next rather than saving it." Dr T Martin

13. “Use the TRAP algorithm when making subsequent treatment decisions. T=Timing of relapse; R=Response from prior therapy; A=Aggressiveness of disease; and P=Performance status. Dr SV Rajkumar
14. “Teclistamab typically requires an initial minimum 7-day hospital stay, requiring 3 step-up doses, 48 hours in between each. However, if an out-patient clinic (such as at Mayo) has immediate access to hospital treatment, a patient may be treated as an out-patient.” Dr Yi Lin
15. I listened to several talks on Decentralizing Clinical Trials. Rebekah Angrove, PhD, stated: “The number one reason for patients not participating in Clinical Trials is because they were never asked.” That’s a lesson for us patients that we should ask our oncologist if there’s a clinical trial we should consider.
16. “If the financial impact is similar, our facility prefers using Denosumab over Zometa since Myeloma patients are prone to kidney disease.” Dr N Raje
17. “In very early analysis, sequencing BCMA therapy (Blenrep, bispecifics) followed by a BCMA CAR-T appears to produce less effective CAR-T results, whereas the reverse appears not to be true.” Dr J Berdeja
18. “Will CAR-T up front replace SCT? We hope to answer in the next years.” Dr S Lentzsch
19. “The management of Myeloma is a marathon, not a sprint.” Dr P Richardson
20. “I favor #downwithdex but #ditchthedex and #darnthatdex are also encouraged” Dr J Mikhael
21. “Following a CAR-T the cancer center needs to work closely with the referring physician who may need to address side effects such as cytopenia.” Dr A Krishnan
22. “Iberdomide appeared so free of side effects that one of my patients thought he was in the placebo arm.” Dr S Lonial

### **MGUS & SMOLDERING MM (early screening)**

23. iStopMM (Iceland). [See [www.myeloma.org](http://www.myeloma.org) for full explanation of iStopMM.] IgA MGUS behaves in contrast to other immunoglobulin subtypes with prevalence rising slowly with advancing age, if at all after age 70. [T Love, 103]
24. iStopMM (Iceland). After examining 1,814 MGUS pts, there was no evidence of MGUS progression after Covid vaccination. [R Palmason,105]
25. iStopMM (Iceland). They have developed a model to predict  $\geq 10\%$  Bone Marrow Plasma Cell (BMPC). Predictors are all accessed via blood (e.g. M-protein, IgG, IgA, IgM, FLC ratio). As such, many MGUS patients could defer Bone Marrow Sampling. [E Eythorsson, 107]
26. GEM-CESAR for HR SMM: N=90 pts did KRdx6-> SCT -> KRdx2 -> R up to 2 years. 95% ORR. 23% of these patients were MRD- (NGF  $10^{-5}$ ) 4 years after the SCT and 2 years after completing treatment. Could these patients be cured? [MV Mateos, 118]

27. Results of the 2-yr ASCENT trial (Dara-KRdx12-> DaraRx12 maintenance) for HR SMM N=87 pts were updated. 55% of pts have completed the full 2 years while 14% of pts went off study for reasons like personal/physician decision, adverse events, progression, and 1 death. ORR is 97%, 84% have become MRD-, and 3yr PFS is 90%. So, are any of these patients cured? They'll need to be followed for 10-15 years before that question can be answered. [S Kumar, 757]

## FRONTLINE (INDUCTION OR FIRST LINE) THERAPY

### TRANSPLANT-Eligible

28. From the Canadian Myeloma Group database, they examined 3821 myeloma patients who had an ASCT (8% had tandem) as frontline therapy during 2007-2021. Most induction was CyBorD (72%). mPFS about 36 mos (std-45; HR-28). 54% of pts received maintenance (mostly Rev). With Rev maintenance, mPFS=54 mos and mOS=159 mos (that's 13+ yrs), which is a 4 yr OS improvement over no maintenance. HR maintenance had mOS 97 mos (64 mos with no maintenance). [J Cole, 117]
29. For Ultra HRMM (>1 HR factor or SKY92 genomic risk) and primary PCL pts, this treatment includes a transplant followed by 18(!) cycles of Dara-VR/d consolidation before DR maintenance till progression in a study called OPTIMUM. Results were favorably compared with ultra HR patients from the Myeloma XI trial with less, but still substantial treatment. For example, looking at about 100 comparable pts in each study, the PFS estimate at the end of consolidation (that's 30 mos) was 78% compared with 30-month PFS of 40% in Myeloma XI. And while results are early, 30mos OS is positive early at 84% v 74%. Prevention of relapse remains the key challenge for ultra HR, even for those that become MRD-. [M Kaiser, 758]
30. Another HRMM study for both TE (SCT included) and TNE (no SCT) that used Isa-KRd for induction, consolidation (4 v 6 cycles), and Isa-KR maintenance of 26 cycles. For N=99 and 26 pts respectively, ORR rates were 95% and 89%. However, PFS data wasn't provided so there's certainly more to learn. [K Weisel, 759]
31. A retrospective analysis comparing VRd with KRd induction for HRMM using 67 and 87 pts respectively from MSKCC. The groups were well-balanced, each having about 74% 1 HR factor and 26% >1 HR. ORR at the end of induction was 93% and 98% for VRd and KRd respectively. mPFS were 41 and 71 mos while 5yr OS was 63% and 85% respectively. [C Tan, 752]

## MAINTENANCE

32. How long should patients take maintenance treatment after a transplant? This study looked at patients in the large Myeloma XI trial. It concluded that there's less value in the 5<sup>th</sup> year of maintenance than years 1-4, so perhaps there's a stopping time between years 4 and 5? If the patient had sustained MRD-, the data showed that they should still get maintenance for 3 years. Newer trials randomizing patients after sustained MRD- are needed. [C Pawlyn, 570]
33. MRD2STOP is the name of a study that examines patients after 1 year of maintenance therapy and enter this study to further examine PET and MRD- at both  $10^{-6}$  and prospective  $10^{-7}$  assessment. Of the 70 patients screened, 38 pts (39% with HR MM) met these negativity criteria and have stopped maintenance. After 15 mos, 33 pts have had no MRD progression. It was also

noted that over \$9M is saved by stopping Rev maintenance after 15 mos. Of course, longer follow-up is needed. [B Derman, 870]

### **TRANSPLANT-Ineligible**

34. A “dex-sparing” regimen of Dara-Rev (DR) in frail NDMM patients was compared with Rev-dex (Rd). DR showed better ORR (96% v 85%) but PFS analysis is on-going. Personally, I was disappointed this study didn't use patient PRO's. And DRd might have been a more informative arm. [S Manier, 569]

### **CURRENT TREATMENTS FOR RELAPSED/REFRACTORY (R/R) PATIENTS**

35. The ICARIA-MM study compared Isa-Pd v Pd and now longer-term results are available. One important outcome was that the use of Dara combinations directly after the Isa-Pd appears less effective. [P Richardson, 247]
36. Roughly one-third of CAR-T pts have on-going  $\geq$ G3 cytopenia 4 mos after infusion but the majority recover after 1 year. This could be correlated with older age, prior number of LOTs and prior SCT. [S Thibaud, 249]
37. Once relapsed from a BCMA CAR-T, a subsequent BCMA CAR-T can show high ORR but generally low PFS. Pts may also response to therapies previously deemed refractory but again duration of responses appear limited. It's fortunate that other targets besides BCMA are being examined. [K Reyes, 250]

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

38. KarMMa-2/Ide-cel/Abecma: CAR-T treatment for HRMM pts in cohort 2a (relapse within 18 mos after frontline SCT and maintenance). Treatment 150-450M (median dose 425M cells) Car-T cells. N=37 became 22 evaluable pts. ORR=84%, DoR 15.7mos (23,5 mos for CR pts). mPFS 11.4 mos, 2yr OS 85% was event-free. MRD- at  $10^{-5}$  was 68% in all pts (85% in CR pts). All CRS (84%), only 1 pt grade 3/4. Infections 60% (G3/4 22%, 2 pts G5 who died). All in all, a favorable benefit-risk. [K Patel for S Usmani, 361]
39. BMS-986393 CAR-T that targets GPRC5D(!): RRMM pts, Ph1 first results, 5 dose levels 25M-450M, N=33 ( $\geq$ half prior BCMA, 39% previous BCMA CAR-T). ORR 90% but 100% at the higher doses. Prior BCMA ORR 80%. [J Berdeja for S Bal, 364]
40. GC012F is a BCMA/CD19 dual-targeting FasTCAR-T as first-line TE-eligible High Risk NDMM. N=17. ORR 100%, all  $\geq$  VGPR (88% sCR). All 17 MRD- at  $10^{-6}$  through month 12, long persistence. Only 29% CRS, all G1/2. Also shorter manufacturing 22-36 hrs. Impressive data. [J Du, 366]
41. BMS-986354 CAR-T (BCMA) uses the NEX-T manufacturing process for N=65 RRMM with mLOT=5 and ORR=95.1% as well as CRS 80% all G1/2 except 1xG3 pt. The unique part of this presentation was the manufacturing process of only 1 week, compared with 4-5 weeks for today's CAR-Ts. This is quite important because patients can have significant disease progression (despite bridging therapy) while waiting 4-5 weeks. [L Costa, 566]

42. The original KarMMa study resulted in ABECMA approval and showed a mPFS of 9 mos. This new retrospective study examined pts getting ABECMA after prior BCMA treatment, which was not allowed in the KarMMa study. As such, for these prior BCMA treated patients, mPFS was only 3.2 mos. [C Ferreri, 766]
43. For the KarMMa study, it was shown that MRD- & CR at months 1, 3, 6, and 12 correlate to improvement in mPFS of 12.5, 20, 22, and 30 mos respectively. [B Paiva, 868]

### **BISPECIFICS (myeloma cell X t-cell)**

44. Talquetamab-MonumenTAL-1 (GPRC5D x CD3) given subQ to N=105 pts across 3 cohorts...2 different dosages and a group of previous BCMA treatment recipients. Resulted in ORR 63% (prior T-cell redirection) -74% and importantly low infection rates (All:50-57%, G3/4:12-17%) compared with other bispecifics. FYI, Janssen submitted Talq to FDA early Dec'22 for accelerated approval. Side effects also include mouth and tongue dryness, rash, and nail disfigurement or shedding. [A Chari,157]
45. Elranatamab-MagnetisMM-1 (BCMA x CD3) given every week or every other week subQ at dosages 215-1000mg/kg to N=55 pts heavily pre-treated (including prior BCMA) in the study. This resulted in ORR of 64% (ORR 54% for pts with prior BCMA therapy), mDoR of 17.1 mos. When step-up dosing and pre-meds were implemented, CRS decreased from 87% to 67% with no G3/4, while G3/4 infections occurred in 21% and 5% respectively. [N. Raje, 158]
46. Elranatamab-MagnetisMM-3 (BCMA x CD3) given weekly subQ 76mg with 2-step-up doses to N=123 patients. So far the first week requires hospitalization like Teclistamab. After 2x28-day cycles, dosed every 2 weeks. ORR 61%, 9-mth DoR and 9-mth PFS were 84% and 63% respectively. All CRS (58%) were G1/2. Infections 67% (G3/4 35%). [N Bahlis, 159]
47. Elranatamab-MagnetisMM-5, Part 1 (BCMA x CD3). Elranatamab (44 or 76mg) + Dara (no dex!), both subQ, n=34. ORR 71%, All CRS (47%) G1/2. Part 2 will be Elra+Dara vs DaraPd for RRMM >= 1 LOT. [S Grosicki, 1921]
48. Teclistamab Majestic-2 (one cohort) (BCMA x CD3): Tec+Dara+Rev (no dex!) for N=32 with 1-3 prior LOT. Tec dose was either .72 or 1.5 mg/kg, then 3mg/kg at cycle 3. ORR 94% (>= VGPR 90%). All CRS (81%) were G1/2. Infections 91% (G3/4 38%). Early data. Majestic-7 planned: TecDR vs DRd in NDMM. [E Searle, 160]
49. Forimtamig (RG6234) (GPRC5D x CD3): N=51 (IV) + 57 (subQ), 20% prior BCMA. ORR 67% (>=VGPR 56%). Treatment duration plan is 1 year. ORR for prior BCMA is 52%. mDoR 11 mos. (I've averaged IV and subQ results when small individual differences.) All CRS (80%) G1/2 (2 pts G3). Infections IV all 61%, (G3/4 22%); subQ all 46%, (G3/4 26%). [C Carlo-Stella, 161]
50. Alnuctamab (BCMA x CD3). 2 years ago Celgene/BMS presented results for IV but CRS was high. Developed subQ to lower CRS. RRMM pts with >= 3 LOT. Dose expansion doses are 10 and 30mg. N=68. ORR 53% (>= VGPR 40%), although 30mg ORR 65%. All CRS (53%) were G1/2. Infections all 34%, (G3/4 9%). [S. Wong, 162]
51. Since CRS is a major issue with most CAR-T's and bispecifics, this study provided the bispecific Cevostamab (FcRH5 x CD3) with either pretreatment of Tocilizumab ("toci" often used to treat CRS) or

no pretreatment. The pretreatment arm resulted in lower CRS (39% v 91%) as well as better ORR (55% v 37%). [S Trudel, 567]

52. Another Cevostamab study showed that after 1 year of fixed length treatment, some patients maintained their response a year later but data is small and early. [A Lesokhin, 1924]
53. ABBV-383 monotherapy at 40mg (N=55) and 60mg (N=61) Q3W doses is well tolerated in pts with RRMM. Durable responses (ORR 58%, 61% resp) were observed at both doses, including in pts with triple-refractory RRMM. mPFS was long (13.7, 11.2 mos). CRS 70% all but 1 pt was G1/2. G3 infections were 22%. [P Voorhees, 1919]

### **OTHER Drugs**

54. Modakafusp alfa (“Moda”) fuses interferon (the killing machine) to a CD38 monoclonal antibody (MM cell locator) from Takeda in RRMM pts, N=30 at 1.5mg/kg dose every 4 weeks, and showed a 43% ORR (39% for prior refractory CD38, 27% prior BCMA but 60% no prior BCMA). It had no constitutional or neuro effects seen with the “original” interferon but did have cytopenias. Note that adding dex to Moda didn’t seem to make a difference. [D Vogl, 565]
55. Mezigdomide (“Mezi”) is one of the CelMods from BMS/Celgene, more powerful oral therapies than their earlier IMiDs Rev and Pom. For N=101 RRMM pts with  $\geq 3$  LOT, Mezi (1 mg/day 1-21) plus dex was given. ORR=41% (30% for pts with plasmacytomas, 50% for pts with prior BCMA). Going forward, Mezi will be combined with Kd, Vd, and Dara. [P Richardson, 568]
56. The other CelMod is called Iberdomide, which is less potent, so may be used earlier while Mezi gets used later. A study with Iber (1.6 mg/day 1-21) + dex for RRMM N=41 with prior anti-BCMA therapy showed ORR 34.1%, mDoR 7.5 mos, and mPFS 2.3 mos. [S. Lonial, 1918]

### **MRD & Mass-Spec**

57. Circulating clonal plasma cells (CCPC) are potentially cells found in our blood stream at diagnosis. Quantifying these using multicolor flowcytometry provides an independent biomarker for the prediction of PFS and OS, perhaps being more informative than ISS, R-ISS and other MM staging guidelines. [P Tembhare, 469]
58. Circulating Plasma Cells (CPC) was shown to perhaps be a better prognostic factor than BM Biopsy/Aspirate for NDMM patients. [E Terpos, 647]
59. There was a whole session (6 oral presentation abstracts 865-870) that focused on new approaches (e.g. BloodFlow  $10^{-8}$ , QIP-Mass-spec-Exent) to MRD testing, including new techniques to use peripheral blood and hopefully reduce the number of bone marrow biopsies.

## **DIVERSITY, EQUITY, AND INCLUSION (DEI)**

If you've seen my ASH summary from previous years, you'll recognize this as a new section. But ASH focused on DEI this year more than ever and so will I. In fact, it began with an excellent Education Spotlight session on "Underrepresented minorities in clinical trials...". It was chaired by MM expert Dr K Anderson and included talks from Drs L Costa and S Ailawahdi, as well as Dr Rayne Rouce. Why is this such an important topic? Dr Costa said "Proper clinical trial population representation is necessary for both internal and external validity." If Blacks are twice as likely to get MM as Whites and represent 20% of MM cases but < 5% of MM trial participants, then our trial results may not be externally valid.

How do we fix this? It will be difficult. Dr Costa showed a slide that indicated income levels and NCI centers which run trials are not necessarily in Black population areas. Many potential strategies were suggested by Dr Ailawahdi (e.g. setting targets, updating inclusion criteria, prespecifying race subgroup analysis, supporting community engagement, expanding trial locations and more). Dr Ailawahdi noted "As more expensive niche MM drugs come out, disparity may increase [so we need to do something sooner rather than later]." And Dr Rouce provided strategies for increasing diversity in the medical field, starting with kids at the high school level. The area of diversity had more than a dozen abstracts focus on this difficult but necessary-to-fix issue. Here are some of those abstracts under subtopics with brief summaries:

### Risk Factors

60. Velcade-induced neuropathy higher in Blacks. [L Sun, 3173]
61. Black treatment outcomes similar to Whites, even though disparity in access and Socioeconomic Status (SES) [J Kort, 3224]
62. Self-reported race and genetics need to be assessed when investigating race and MM [P Blaney, 174]
63. Young AA adults (<46yo) factors compared to Whites: more MM, lower del13 & gain 1q, as well as better PFS [M Saldarriaga, 4469]
64. Higher prevalence MGUS detected by Mass Spec (13%) for AA>49yo [D Lee, 3216]
65. Higher sFLC in AA-MGUS. Genetic, socioeconomic, environmental impact? [L Bertamini, 4495]

### Clinical Outcomes

66. Mortality rates past 20 yrs: AA highest, Asians lowest. Age-adjusted Per 1M Persons AA (62), W (31), PI (23), and Asian (16). [A Zubaidi, 4513]
67. Hispanics have lower improvement in OS trends than other race subgroups. [F Anwer, 4904]
68. Small CAR-T numbers but for 215 Abecma pts (70% W, 17% B, 10% H), Blacks were more likely to develop CRS, have longer hospital stays, more cytopenia, worse PFS. [L Peres, 252]
69. Non-hispanic Black and Hispanic survivors may benefit from interventions targeted to asses and improve sleep and mental health as well as symptoms of racism. [K Karvonen, 382]
70. If enrolled in Part D Medicare. Blacks had better survival than Whites. Otherwise no OS differences. [R Wang, 2309]
71. Given other factors equal, Hispanics were found to have a 2.5-fold higher incidence of del-1p which may account for lower PFS. [K Cicero, 3582]
72. An analysis at the end of the Griffin trial showed better sCR & MRD- outcomes on the Dara arm for both B & W; however lower 48-mos PFS for Blacks, who had higher discontinuation due to AE's. [A Nooka, 4560]

## Barriers to Care

73. Barriers included inadequate education and personalizing of treatment plans and ineffective Shared Decision Making-being worse for Blacks and Hispanics than White [J Mikhael, 2235]
74. Improving patient-clinician relationships (trust is critical) and clinical trial availability in the community, support to help with logistical barriers and addressing physician biases are needed to improve clinical trial enrollment [S Grant, 380]
75. Data showed that a higher Social Vulnerability Index (determined by the CDC) was associated with lower PFS while race, insurance payor, and urban/rural location had no significant association with PFS. [K Salafian, 4907]

## OTHER RESULTS

76. These abstracts both focused on Quality of Life (QoL) issues as determined by Patient Reported Outcomes (PROs):
  - A) For frail patients, QoL benefits were seen in the MAIA study comparing DRd with Rd. The Dara arm showed benefit in pain symptoms and global health over Rd alone while both arms improved fatigue, emotional and social functions. [A Perrot, 472]
  - B) For transplant eligible patient, the Griffin trial (Dara +/- [VRd->SCT->VRd->R]) PRO analysis concluded that the Dara arm resulted in greater improvements in health-related QoL, with a notable reduction in pain. [R Silbermann, 473]

## 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.

For someone diagnosed with stage III MM 28 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 14 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. ASH2022 highlighted the tremendous advances we have made in treating this cancer for both the newly diagnosed and relapsed patient. That said, for the majority of patients, multiple myeloma continues to be a frightening cancer requiring long-term treatment and frequent monitoring for the rest of the patient's life.

**GLOSSARY (according to Jack)**

<p><b><u>Drug (brand names) by Drug Class/Category</u></b></p> <p><b><u>IMiD – Immunomodulatory Drug</u></b>  T – Thalidomide  R – (Lenalidomide) Revlimid  Pom – Pomalidomide (Pomalyst)</p> <p><b><u>PI – Proteasome Inhibitor</u></b>  V- Velcade (Bortezomib)  Cfz, K – Carfilzomib (Kyprolis)  I, Ixa – Ixazomib (Ninlaro)</p> <p><b><u>mAb – Monoclonal Antibody</u></b>  D, Dara – Daratumumab (Darzalex)  E, Elo – Elotuzumab (Empliciti)  Isa – Isatuximab</p> <p><b><u>HDAC - histone deacetylase inhibitors</u></b>  Pano – Panobinostat (Farydak) but no longer FDA approved in the US</p> <p><b><u>Steroids</u></b>  P – Prednisone  D or d - Dexamethasone</p> <p><b><u>Chemotherapy Drugs</u></b>  C – Cyclophosphamide (Cytosan)  M – Melphalan</p> <p><b><u>Treatment Measurements</u></b>  EFS – Event-free Survival  ORR – Overall response (&gt;=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</p>	<p><b><u>Treatment Response</u></b>  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 &amp; 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<sup>-5</sup> or 10<sup>-6</sup>)</p> <p><b><u>Side Effects</u></b>  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</p> <p><b><u>Tests/When to treat?/Other</u></b>  CRAB – High Calcium, Renal, Anemia, and Bone...  CRABi – CRAB + “i” increased infections  FLC – Free Light Chain</p> <p>SCT – Auto stem cell transplant.  TE, NTE – Transplant Eligible of Not TE</p> <p>LOT – Lines of Therapy</p> <p>TE, nTE – Transplant eligible or non-TE</p>
<p>“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 &gt;20% plasma cell, &gt;2 M-spike, &gt;20 FLC ratio  RP2D – Recommended Phase 2 Dosage</p>	