

**IMW 2015, Rome, Sept 23-26, 2015**  
**Jack Aiello, Myeloma Survivor Dx'd 1995**

This is my second time attending an International Myeloma Workshop (IMW) meeting which is held every 2 years. This 4-day meeting consists of nearly 3000 attendees, mostly hematologists (70%) with smaller numbers of pharma reps (15%), researchers, and nurses. This 15th IMW meeting contrasts with the first one held in 1987 with 34 attendees (including Drs Robert Kyle and Brian Durie).

**Major Discussion Topics**

Economic Concerns (aka Drug Costs) versus Innovation and Quality of Care was the initial lecture and was referenced throughout the 4 days. Dr J-L Harousseau indicated the health industry has 2 challenges of Increased Life Expectancy and Increased \$\$ for Innovation which make it very difficult to reign in prices. However, US prices for Revlimid (\$13.7K/cycle), Velcade (\$6.6K/mo) and Thalidomide (\$4.9K/mo) seem outrageous. So many questions: What is a fair price from Pharma? How do Health Orgs such as the FDA assess the Incremental Cost Effectiveness Ratio (ICER = Cost/QALY, which is Quality Adjusted Life Years)? Is it the Physician's responsibility/burden to consider costs when suggesting treatment choices? Should Payers cover the cost to treat a disease rather than cost to pay for a drug? Perhaps Minimum Residual Disease (MRD) measurements will help guide treatment courses as well as treatment costs (e.g. should MRD- mean a shorter duration of maintenance?). So much more needs to be done.

Speaking of MRD, it was also discussed throughout the meeting. NGF (Next Generation Flow, 2x8-color tubes, although I also heard 10-color) requires a fresh bone marrow sample while NGS (Next Generation Sequencing) can use frozen samples. Both seem to have 10<sup>-6</sup> accuracy with NGF costing less. One meta-analysis from Dr. N. Munshi examined 21 studies which used MRD (less accuracy than 10<sup>-6</sup>) to examine 500 patients considered by blood tests to be in a CR (Complete Response). It turns out that one-third of these pts were MRD+. MRD- showed better PFS (60/36mo), OS (Not reached/82mo) and 5yr OS (78/60%). Remember, all these pts were in CR. It is therefore obvious that MRD- is a much better goal than CR.

There are fewer breaking news announcements at this meeting compared to ASH and ASCO. More instructional presentations are provided such as revised IMGW criteria for MM/SMM and a reminder that MRI detects focal lesions better than lytic lesions.

NDMM-Young Pts: (1) Dr M. Attal broke news that the French part of the IFM/DFCI DETERMINATION Clinical Trial shows better PFS for early SCT, so SCT will likely remain the standard of care (more details at ASH). (2) Dr A. Jakubowiak said of his Ph 2 trial (75 pts) KRd +/- SCT that the SCT arm improved CR by 40 points and is trending toward better PFS and OS results. Optimal induction: Probably 3 drugs but perhaps mAb will make it 4. Dr H. Einsele showed that allo transplants for High-Risk pts provided benefit. Dr M. Cavo said that 40-50% of pts fail to achieve a CR after an SCT, thus the need for consolidation which increases CR by 10-20%. Dr. P. McCarthy said that Velcade maintenance is particularly beneficial for pts with renal

failure and/or 17p-, while Dr S Giralt said that 70% of US pts received Revlimid maintenance after an SCT.

NDMM-Elderly Pts: Dr S. V. Rajkumar said "For pts  $\geq 75$ yo, just give 20mg dex/week" whereas Dr P. Richardson explained we need to "throw a net" over the MM to catch evolving clones. In the near future, this "net" might be all oral RId (Rev-Ixazomib-dex). And we might even add an mAb Elotuzumab, Daratumumab, or SAR (Isatuzimab). Apply the best possible treatment at all stages of treatment. Dr. A. Palumbo has published data on developing treatment adjustments for Fit-Unfit-Frail pts, which can be scored at [www.myelomafrailtyscorecalculator.net](http://www.myelomafrailtyscorecalculator.net) developed by IMWG.

Relapsed/Refractory MM Pts: There were talks on treating R/R MM pts including those with Extramedullary Disease and Serious Adverse Events as well as providing Palliative Care.

Futures: Dr K. Anderson summarized that IMiDs, PI's, mAb's, Checkpoint Inhibitors, Vaccine, and CAR-T (the latter 4 being Immunotherapy) will all play a role to make immune systems more effective. He noted that mAbs against CD38 might be safer than CAR-T for CD38 since CAR-Ts are so powerful and CD38 is found elsewhere on other cells besides MM. "BCMA might be a favorite target." Dr E. Stadtmauer updated the UPenn CD19 CAR-T for 10 MM pts: so far 1 pt has had a long, great result, 1 relapsed, others are too early to say. Finally Dr J. Zonder spoke about bi-specific Antibodies (bsAb) designed to be both a receptor and signaler on an MM cell or perhaps receptors between MM and NK cells. He said "It's never been a better time to be a mouse with MM." I can't wait to see all this translated to the clinic.

Pharma companies sponsored 90 minute symposiums within the IMW agenda. Novartis speakers discussed HDAC inhibitors including Panobinostat studies, indicating increased efficacy when combined with PI's and IMiDs as well as probably future mAb's and CAR-T's. Amgen featured talks on Proteasome Inhibitors (\*\*\*)although I missed this section due to AMN meeting...discussed later). Celgene focused talks on future role of IMiDs. Janssen (Dara) sponsored talks on mAb's. Dr S. Lonial said "mAb's are risk-agnostic." Dr P. Moreau talked about IRR events (Infusion-Related Reactions) for Dara...nasal congestion, throat irritation, cough, chills so give pre-meds to avoid. If IRR occurs, stop infusion and resume at half-speed drip. BTW, Dara can actually add to IgG results so SPEP may be less accurate resulting in a new blood test called DIRA. A better blood test might also be needed for other mAb's.

Other interesting agenda item are presenters assigned to debate sides of certain topics: Should Therapy change for High Risk versus Low Risk pts? Should MRD/Imaging or FISH/Age guide treatment? Dr. O. Landgren pointed out the best responses to KRd are at 5.5 cycles so perhaps the "standard" 4 induction cycles should be 6. Or maybe MRD can correlate treatment with number of cycles. Or perhaps we should automatically add 2 cycles after reaching MRD- (up to 8)? Dr P. Sonneveld said Age reflects pt condition; FISH pt prognostic risk before tx; MRD pt condition after tx. He noted that a patient who has MRD- w/o FISH cytogenetics does better than MRD- pt w/ FISH cytogenetics.

Other debates included: Can we cure MM by 2020? [Dr B Barlogie said we already have.] Should newest agents be combined or given in sequence? I find these debates entertaining, and of course, there's no one right answer. Perhaps when we get to Precision Medicine there will be.

Trials: (1) Described by Dr P. Forsberg for NDMM pts: Kd (2 cycles) -> BiRD (2 cycles) [-> SCT] -> R maint 10mg. Induction results so far ORR 90% (64%  $\geq$  VGPR) which is great considering half the pts were High-risk. Some cardiac events at the K 56mg/m<sup>2</sup> dose (rather than 45 mg/m<sup>2</sup>). (2) Dr A. Spencer discussed Ph1 PMd (Pom-Marizomib-dex) for RRMM pts with prior Rev, Vel and half Cfz. Interim results at the end of cycle 1, 10 of 14 pts showed some response (so response is rapid) and ORR 62% which has increased to 71% with Ph2 dosage. He also indicated that oral Marizomib (another PI) will be entering Ph1.

Posters: 1) A 5-drug induction regimen ACVDL (Adriamycin, Cytosin, Velcade, Dex, and Rev) showed good ORR (80%) using lower Rev (15mg) which may benefit pts with ASEs from Rev 25mg. 2) An early Ph 1/2 study with another CD38 mAb MOR202 in RRMM pts is showing single agent responses and will be combined with other drugs in future trials.

Finally, the IMW agenda also included presentations by Susie Novis-IMF and Daniel Auclair-MMRF. Speaking of the IMF, preceding the IMW mtg, I attended a meeting of the IMF's Global Myeloma Action Network (GMAN). Perhaps 15 countries, mostly European, had Myeloma advocates there to discuss their own organizations and learn from each other. While we in the US face exorbitant drug prices, we have it much better than many countries with limitations on drug access, fewer myeloma experts and practices, strong government controls and more.

(\*\*\*) I mentioned that I missed the Takeda sponsored event because the IMF invited me to attend a 2 hr meeting of the AMN (Asian Myeloma Network). I found it quite fascinating to watch MM docs from China, Japan, S. Korea and other countries report on current Asian trials and develop new ones. I learned that IgD MM has twice the occurrence in Asia as compared with the US and the average age of MM at diagnosis is 62yo in Asia, compared with 69yo in the US.

PS. I try to be accurate with my note taking but material is presented quickly. If you have any questions, please feel free to email me [jackaiello@comcast.net](mailto:jackaiello@comcast.net).