I attend this meeting as a result of being on the Consumer Advocacy Council (CAC) of the Center for International Blood and Marrow Transplant Research (CIBMTR...www.cibmtr.org). This conference is an annual combined scientific program between the CIBMTR and the American Society for Blood and Marrow Transplantation (ASBMT...www.asbmt.org), thus the word "Tandem". BMT CTN (Blood and Marrow Transplant Clinical Trials Network) is the clinical trial arm of CIBMTR. They have enrolled >7500 patients in USA transplant center trials. And the CIBMTR itself is a research collaboration between the Nation Marrow Donor Program (NMDP, Be-The-Match) and Medical College of Wisconsin (MCW).

And as you can guess from the names of these organizations, this conference is all about TRANSPLANTS for blood cancers and blood disorders such as myeloma, aplastic anemia, sickle cell disease, lymphoma, leukemia, etc. This conference is held for doctors, nurses, hospital pharmacists, BMT trial coordinators, and researchers that work in cellular therapy and BMT, and over 3100 from around the world attended this year. It's similar to ASH (American Society of Hematology) with abstracts presented orally or via poster and exhibitors, but on a much smaller scale. For example, ASH has 25,000 attendees with 800 abstracts just for myeloma whereas this Tandem BMT meeting had 600+ abstracts for all blood cancers (all in connection with transplants).

I also attended meetings specifically relevant to the CIBMTR, which keeps a database of transplant records (100% of all allo's (required by federal law) and 80% of auto's (not yet a federal reporting requirement)) resulting in information on >425K patients. This data can be analyzed by statisticians as requested by investigators trying to answer questions such as "comparing inpatient versus outpatient results" or "predictors of relapse from allo's for Myeloma". I also attend Working Committee meetings that recommend, discuss, and vote on approvals of research proposals, some of which result in patient summary write-ups posted to the CIBMTR site. These summaries can be found at: https://www.cibmtr.org/ReferenceCenter/Patient/PatientSummaries/pages/index.aspx. Finally, I attended myeloma-specific meetings such as the BMT CTN Myeloma Intergroup Meeting, chaired by Drs Marcelo Pasquini (MCW) and Amrita Krishnan (City of Hope), and focused on current and proposed myeloma trials.

Since this is a meeting on transplants, it’s important to know that most allogeneic transplants (allo's) are done for AML, ALL, CLL (leukemias) while most autologous transplants (auto's) are done for lymphomas and myeloma. While the source for an auto transplant is the patient themselves, the allo has several possible sources, all of which are potential studies for efficacy, side effects profiles (on both the patient and donor), and availability. These donor sources include: sibling matched, sibling unmatched, parent/child half-matched (HAPLO), matched & mismatched unrelated (MUD/MMUD) and cord blood. Stem cells can be extracted from both the bone marrow (20% graft source) and peripheral blood (80% graft source). Interestingly CIBMTR studies have shown significant differences in both engraftment efficiency and the degree of GVHD (Graft Versus Host Disease) depending on the location of graft harvest. Allo transplants can be myeloablative (full) or non-myeloablative (mini, reduced-intensity-conditioning, also known as RIC-allos).

Most myeloma transplant discussions began by reminding attendees of the recent ASH presentation given by M. Attal, MD of the French results for the IFM/DCFI 2009 study. He announced there was a clear Progression Free Survival (PFS) benefit seen in patients randomized to the transplant-now arm compared with the transplant-delayed arm. As such, transplants for MM patients is still a hot topic (especially at a transplant meeting with transplant docs).
Some quotes and findings

1) While the US has yet to report on the IFM/DCFI 2009 trial, it was noted that the French side of the study also showed 6 of 54 pt (11%) in the transplant-now arm vs 1 of 48 pts (2%) in the transplant-delayed arms developed SPM’s (Secondary Primary Malignancies), mostly AML/MDS.

2) Both Stanford and UCSF are still recruiting Newly Diagnosed MM pts for the US part of the IFM/DCFI 2009 trial called DETERMINATION. At 537 accrued and randomized of 660 pts, expected to complete accrual by year-end. Dr. P. Richardson

3) I heard a lot regarding MRD for MM and it seems that NGSequence seems to be preferred over NGFlow. While NGS costs more and requires one to have an initial sample at diagnosis (or at relapse), NGF must be done within 24 hrs and is subject to more interpretation (although I’ve heard software is being written to overcome this drawback). Both still require bone marrow samples for analysis.

4) Checkpoint inhibitors such as Pembrolizumab that break the connection between antigens PDL1 found on both MM and Dendritic cell and PD1 found on T cells enables T cells to better locate and destroy MM cells. There’s even interest in combining CAR-T and Checkpoint Inhibitor therapies.

5) Less than 50% of transplant-eligible MM pts get a transplant. P Hari. And S. Giralt reported that only 30-40% of patients who would benefit from ASCT are actually getting it. Top reasons: 72% of pts fear side effects and 50% wait for the disease to progress. Also “lack of referral to transplant doc”. Do you agree?

6) To reduce Oral Mucositis from SCT, use “cryotherapy”, i.e. chew ice before, during and after melphalan infusion. P. Hari, others

7) Drs Ken Anderson (DFI) and Joseph Mikhael (Mayo) gave a wonderful presentation on the Management of MM Using Emerging Therapies with an SCT for both newly diagnosed and relapsed pts. Dr Anderson displayed results from 2 trials that showed SCT vs non-SCT 5-yr OS % for ISS I/II 85% vs 72% and Standard Risk 84% vs 72%. And maintenance vs no maintenance 5-yr OS% was 77% vs 60%. Dr. Mikhael said “Daratumumab will have the greatest impact of any drug approved in 2015.” He also reminded attendees that while Elotuzumab + Rev has been an effective combination, results of Elo + Velcade have been less impressive.

8) “We know that the 2nd SCT generally offers 50-70% PFS of the 1st SCT.” J Mikhael

9) “At Mayo, the first infusion of Dara lasts 9 hours and 60% of pts have reactions during that first infusion. Then it gets better.” J Mikhael

Some MM discussions

10) As a reminder, transplants for myeloma patients are almost always auto’s with stem cells harvested via the peripheral blood (apheresis). However, various types of allo transplants for MM patients are still an option, typically within clinical trials. What about that bag of stem cells...do they get infused as is, or are they treated in some way to remove any residual myeloma cells? It has been shown that CD-34 bead selection of graft source MM cells (to lower the amount of myeloma cells re-infused) not only does not lessen myeloma relapse, but it also slows engraftment of healthy cells.

11) Melphalan has challenges in terms of both pharmacokinetics stability (preparation & time of efficacy) and side effects from propylene glycol (PG). In IV solution, it degrades and loses 1% of its potency every 10
minutes! Companies such as Spectrum Pharmaceuticals are developing Mel-substitutes (Evomela) that can be prepared ahead of time and don’t use PG. This topic was mentioned several times throughout the meeting.

12) Minimum Residual Disease (MRD) continues to be incorporated into clinical trials so that doctors in the future can use MRD results to guide treatment plans. An interesting trial discussed was called MASTER MM trials looking at KRdDara (3 cycles) +/- SCT -> Maintenance of RDara (MRD+) or Dara (MRD-). P Hari

13) In addition to the above, Dara continues to be incorporated into new proposals, e.g. Pom-d-Dara induction for HR MM. P Stiff

14) Perhaps a future IMF/DFCI2017 trial would incorporate MRD endpoints, induction of Rev-Ixa-d (Rid) + Dara, a 2nd SCT option (at least in France who already believe the 1st SCT is mandatory), and Rev vs Rev-Dara maintenance. P Richardson

15) We’ll be hearing more about an open Phase 1/2 trial (begins recruiting April 2016) that examines whether or not the infusion of a dendritic cell vaccine after an SCT further stimulates the immune system to fight myeloma cells. D Avigan

16) A novel consolidation concept was proposed to follow an SCT with Rid and then randomize to R or I maintenance. R Vij

17) In the Plasma Cell Disorders (e.g. Myeloma) working committee, I found 3 of 6 proposed studies interesting but have no idea if any of these or the others will be approved (up to 2). These 3 studies examined a) the incidence of cytogenetic abnormalities by patient race, b) benefit of 3rd transplant, and c) benefit of 2nd transplant. These studies typically take 2-3 years to complete.

18) In the GVHD working committee, I found interesting the proposed studies a) GVHD-free relapse-free survival studies among different donor sources and b) GVHD risk factors and outcomes after haplo transplants. Note these likely have very few MM pts within the data registry.

Some MM poster conclusions

19) Most MM patients > 65yo do not get a 2nd SCT (2-5M cells per transplant), so why harvest for 2 SCT’s? There are no significant differences in SCT responses, PPFS, or OS by ethnic/racial groups or Socioeconomic Status [307]. For 92 NDMM pts who received an SCT + mini allo from 6/6 sibling, results showed PFS of 41% and OS of 62% at 10 years but 22% on immunosuppression at 10 yrs [527].