“All In For a Cure”

Mesothelioma Applied Research Foundation 2013 Symposium

Symposium Report – Liz Darlison
The Mesothelioma Applied Research Foundation (MARF) is the US national organization dedicated to finding a cure and eradicating mesothelioma as a life-ending disease by:

- Funding the highest quality and most promising mesothelioma research projects from around the world through our rigorous peer-reviewed process;

- Helping mesothelioma patients connect with national mesothelioma experts and obtain the most up-to-date information on treatment options;

- Advocating in Washington D.C. for federal mesothelioma research funding to stop this national tragedy.

The work of the Foundation is funded by mesothelioma patients and their families who have invested generously in the search to cure mesothelioma, as well as law firms, drug companies, and companies formerly involved with asbestos, all of whom have joined in the common mission of curing the disease and eliminating the risks of asbestos exposure.

The Mesothelioma Applied Research Foundation funds critically-needed research to develop more effective treatments and ultimately, a cure! They have awarded over $7.6 million in grant funding, advancing mesothelioma science and asbestos research through promising studies and examination around the world. In 2011 the foundations income amounted to $1,988,307 for a full insight into the work of the foundation please review their annual report available at:

http://www.curemeso.org/atf/cf/%7Beb9ec12a-9f10-428a-a38d-189f567fa6a5%7D/AREPORT2011_WEB.PDF

Previously all presentation from the symposium have been posted on the foundations website www.curemeso.org. In addition this year the whole meeting was live streamed on Facebook allowing people all over the world to be involved. Several UK patients and carers we connected and they contributed to the question and answer sections.
Registration for the 2013 symposium opened at 5pm on Wednesday March 6th, 170 delegates were expected.

It was wonderful to meet faces from previous meetings, Anna McCurdy, MARF Board member, registered nurse and widow of Mike who died of Mesothelioma in 2007. Marlyn Landen 13 year pleural mesothelioma survivor, Hanne Mintz Chair of the MARF board who sadly lost her son Adam to mesothelioma to name but a few and of course my friend and colleague Mary Hesdorffer.

Marlyn Landen 13 year pleural mesothelioma survivor.

The events began with a Celebration of Life service led by Reverend Eric Linthicum and Rabbi Barbara Zacky. Doves were the focus of the service with the congregation taking it in turns to place a dove on a tree in celebration of their loved one. Each of those celebrated were called out by name in turn and their photograph was projected for all to see. A poem was read by the daughter Ken Bendix who died in 2007. The service finished with the James Taylor song You’ve Got A Friend.

There was a welcome reception where patients, foundation members and healthcare professionals got to meet and chat. Facebook attendees were welcomed; the whole symposium was streamed live on Facebook so that people could join the meeting from all over the world. UK facebookers were particularly welcomed and I was introduced to them.

The first day started early (as many USA meetings do) with breakfast and registration from 07.00. The MARF board were introduced to the meeting and sponsors were thanked. Over breakfast I met Dr Dirk Brockstedt from Auro Biotech a company that are currently running an early immunotherapy trial using artificially manufactured bacteria in combination with chemotherapy in pancreatic cancer and mesothelioma. We had a chat about the UK mesothelioma community and our experience with trials in particular recruitment. I explained we have a great communication network both through health care professionals and patients and carers and my experience with
recent trials in UK (ADAM and NGRO15) was that we recruited in an excellent timely manner. Dr Brockstedt is going to send me his companies trial portfolio and although they had not previously considered opening trials in UK (despite our high Meso incidence and excellent health infrastructure for trial management) I encouraged him to take back to his colleagues what I had told him and said I would add him to the Mesothelioma UK circulation list and pass his details and the trials portfolio onto Professor Dean Fennell.

The meeting separated out into breakout sessions for bereaved, carers and patients, I was not involved in these. In the main meeting room Mary Hesdorffer did an hour long session called ‘New Patient’ introducing mesothelioma in its entirety. Interestingly and as previously reported from my attending MARF’s annual symposium clinical trials feature significantly in the treatment pathway in the USA and Mary weaved the trials that are open in the USA fully into her presentation.

A 2 hour session followed looking at ‘News from the genetic front’ chaired by Dr Joseph Testa. Dr Testa explained the difference between the types of genetic alteration in cancer, hereditary and acquired (somatic). Hereditary is present in all body tissue and acquired is restricted to tumour cells. Chromosomes of mesothelioma typically have multiple recurrent genetic losses. Dr Testa discussed the hereditary susceptibility to mesothelioma the rationale being that mesothelioma clustering is observed in some families. Studies of families with high incidence have helped identify a new susceptibility called the BAP 1 Cancer Syndrome which appears to predispose to mesothelioma, Uveal melanoma (eye), and cutaneous melanoma.

Dr Testa introduced Dr Harvey Pass surgeon from NY who presented on his work on designing innovative trials to try and identify biomarkers for asbestos and mesothelioma. Dr Pass as a surgeon is eager to develop means of diagnosing Mesothelioma as early as possible, biomarkers offer a means of doing this. Dr Pass reviewed work that has been done to identify mesothelioma biomarkers including mesothelin, osteopontin and FBLN3. Part of establishing biomarkers involves ensuring findings can be replicated by other teams. Dr Pass and his team hope to develop a commercially usable set of biomarkers in meso; current plans include the establishing of a consortium of centres to validate the biomarkers and to lobby for research to study the biomarkers in more detail.

Dr William Harbour, Ophthalmologist from Miami was then introduced; he discussed his initial work that identified the BAP 1 mutations in Uveal Melanoma and how this went on to link with families with mesothelioma.

Dr Haining Yang from the University of Hawaii talked then about the role of HMGB1 in asbestos exposed and in mesothelioma. HMGB1 is a unique protein that usually stays in the nucleus of cells. Once released outside the cell it drives inflammation that can lead to cancer development. When cells are exposed to asbestos HMGB1 is released from the cells. This has been demonstrated in mouse models and increased levels have been found in the blood of asbestos exposed individuals.
It is conceivable therefore that if they can target the inflammatory process novel therapies could be designed to prevent cancer development in asbestos exposed individuals. HMGB1 is highly expressed in mesothelioma cells so targeting it may have a role in treatment too. The first study to look at HMGB1 in more detail is focusing on securing the role of HMGB1 as a biomarker in mesothelioma and a second trial is hoping to study HMGB1 as a potential target for treatment in mesothelioma. Dr Yang completed her presentation talking about the previously reported work regarding the potential role of aspirin, as an anti-inflammatory, in preventing cancer and how this may support the HMGB1 findings and further investigations. A patient in the audience asked if any work had been done to look at the levels of HMGB1 in long term mesothelioma survivors, Dr Yang said not but they would like to. MARF has a register of long term survivors and pledge to link Dr Yang with them in the hope that a trial to look at this could be developed.

Dr Laura Ferris, Assistant Professor of Dermatology picked up on the BAP1 mutation story from the work that she has been involved with in individuals with a familial melanoma. Those from BAP1 families have quite unique features in that they are a rare subtype of epithelial tissue type and do not behave in the same way as other melanomas, for this reason they have renamed this sub type at MBAIT’s, most will not progress to melanoma.

Dr Jill OHar from North Carolina presented about BAP1 in sporadic mesothelioma: Preliminary Report. Dr OHar explained her hypothesis that there are likely host factors that influence mesothelioma development such as age you were first exposed, genetic susceptibility, immunology, sex and latency. To look at this several years ago Dr OHar started to collect blood from her patients and she is now working in collaboration with the BAP1 group and with funding from MARF they are part of the consortium that share their banked specimens and are looking to validate findings. Dr OHar explained that after looking at their population (4000 Meso patients) and wanted to look at their families’ range of incidence of cancer. They developed a cancer epidemiology scoring system to quantify this that gave points depending on who in your family developed cancer. They are currently sequencing specimens from their cohort of patients and the controls. The study is on-going and they appealed for more patients to enrol in the study.

The final presenter for this session was Dr Michele Carbone who summarised what the significance of BAP1 is in mesothelioma. He explained that discovering this presence of BAP1 mutation in Meso offers a potential pathway to target for treatment in Mesothelioma. Genetics is just one factor but there are others such as the inflammatory process, if we can delay development or progression of cancer until a person is much older this is a significant advancement. All of this work depends of teamwork even across tumour types as demonstrated here today with having a dermatologist and ophthalmologist presenting. The MARF foundation has been instrumental in helping develop the collaboration necessary to develop the team approach and for reaching out to patients with a family history of mesothelioma.
Dr Testa closed the session explaining some of the current issues faced within the BAP1 story. There are numerous research and trial issues but also patient/carer related ones too. Some patients initially wanting to be involved in testing withdrew because they worried about their children’s ability to get insurance. Law firms have raised the issue about insurers using this to avoid paying compensation.

An hour and half lunch followed allowing people ample opportunity to network and ask questions of some of the experts.

The afternoon session opened with Jessica Barker, Director of Government Affairs from MARF talking about advocacy. A computer was set up at the symposium in the main room for delegates to take the opportunity to contact their local representatives about the need for Mesothelioma research funding. In 2011 the National Cancer Institute awarded 23 mesothelioma research grants but explained the amount will be cut by 5.1% in this current year.

My presentation followed which provided an overview of the global mesothelioma epidemic.

The next session, chaired by Mary Hesdorffer provided an opportunity for all the studies supported through a MARF grant to be presented.

Dr Tao Dao – Targeting the un-targetable with antibodies

Dr Assunta Rienzo – Identification of Novel Mutation in MPM using deep whole genome sequencing.

Dr Mark Ladanyi – The BAP1 tumour suppressor gene in mesothelioma, new biological insights and new therapeutic opportunities.

Dr Liang Chuan Wang – Personalised Medicine for patients receiving chemotherapy for mesothelioma.

Dr Nadia Zafferoni – Identification and validation of micro RNA’s as a novel biomarkers and therapeutic targets in diffuse peritoneal mesothelioma.

Dr Lee Krug moderated the next session ‘Pharma Speaks Up’ which allowed for the first time two drug companies to meet with patients and present their data. The first was from Dr Julie Maltzman from Morphotek who looked at Amaxtuximab in combination with standard chemotherapy. The study did not meet its primary end point but what it did expose was a correlation between some
biomarkers and participant survival MPF, CA125 and Mesothelin levels all correlated to survival and the company are now putting together a protocol to set up a randomised control trial.

Dr Aimee Murphy from Aduro Bio tech then presented data from their phase 1B study of CRS-207 vaccine and chemotherapy in patients with malignant pleural mesothelioma. The study uses a genetically modified listeria and has recently opened in 3 centres in the USA.

The final afternoon session involved a panel of attorneys in a question and answer type session that was moderated by Erica Ruble fundraising manager for MARF and herself an attorney.

Erica Ruble moderates the legal panel.

**Friday March 8th**

Hanne Mintz chair of the board of directors opened the morning session introducing the MARF board and staff. Melinda Kotzian, chief operating officer reviewed the foundations projects and services and explained about the foundations 501 (not for profit/charity) status. Melinda also described how the foundations $2m dollars annual income is spent.

The majority of the morning centred on a multi-disciplinary panel moderated by Mary Hesdorffer and including Dr de Perrot, thoracic surgeon from Canada, Dr Simone, radiation oncologist, Dr Friedberg, thoracic surgeon, Dr Ettinger, Professor of Medicine and radiation oncologist, Dr Krug,
medical oncologist and Dr Kindler medical oncologist, Dr Michele Carbonne, Professor of Pathology and Dr Robert Kratzke, associate professor of medicine.

Dr de Perrot is involved in trials of neo adjuvant radical radiotherapy; patients have to be suitable for surgical resection as the radiated lung needs to be removed post radiation. Dr Simone spoke about the importance of remaining hopeful and trying to keep a positive outlook, he also encourages a nutritious diet. A UK Facebook question asked the panel why US based studies are not shared more with the UK – Dr Kindler explained there are perhaps some regulatory issues but regardless there is a strong international network and all findings irrespective of where the trial is carried out are shared promptly. Dr Kindler also reassured UK patients that there are a number of trials in development in the UK and there are some excellent UK based researchers working in the UK. UK patients were encouraged to connect with Mesothelioma UK to keep abreast of trial developments in the UK. Mary asked Dr Carbone if he thought we were at the start of exciting times in the treatment and management of mesothelioma and he explained about the progress we have made since the licencing of Pemetrexed and the possibility of personalised medicine is now very likely. Dr Carbone explained how with our increased understanding of cancer biology scientific advances can be translated from one tumour type to another meaning advances should happen much faster, in 10 years time the treatment options will be very different.

There was a lengthy discussion about how patients are getting older and whether or not chemotherapy is appropriate. Doctors on the panel could all recall examples of elderly patients they have treated and Mary has a 92 year old Facebooker who is currently receiving chemotherapy.

The panel were asked if they use chemo sensitivity testing and none of them did.
There were questions from the floor about the growing acceptance of complementary and alternative medicine in the treatment of mesothelioma. Dr Simone, Dr Ettinger and Dr Krug spoke about the potential value of these approaches, patients were advised that they should let their doctor know what they are involved with, that a more holistic approach is valuable and also trusted sources of information about the range of approaches were recommended.

The panel were asked about the value of chemo perfusion/embolization. Dr Krug said he cannot see how this approach would be useful in mesothelioma, it doesn’t make rationale sense. There are some trials looking at intra-pleural chemotherapy and intra pleural gene therapy, these may be of more use.

Dr Carbone was asked about the importance of the BAP1 finding and he explained that this is the first time that we have identified a critical gene that has a role in the development of mesothelioma which opens the door to hopefully better treatments.

The debate about surgical approaches ( EPP v’s LSTP) and the difference in opinion was discussed. Dr Friedberg said the LSTP is an evolving procedure with many different names and no one accepted approach. With EPP everyone is clear about what has been performed. Only a minority of patients are suitable for radical surgery (10-15%) and no one can tell the patient what to do, the benefits are unclear, surgery for mesothelioma remains investigational. Patients have to make their own decision.

Dr Kindler was asked if there were any results available yet from the trial she is leading looking at Tarceva in the treatment of peritoneal meso – not yet!

Dr de Perrot was asked if radical surgery is available in Canada and it is in his centre, patient struggle to get funding for treatment outside of their province and surgery is not available in every province.

A second panel was convened involving Dr Becich professor of biomedical informatics, Dr Krug, Dr Andrew Todd, physicist and director of the Insulators’ Tissue Bank, Dr Carbone, Dr Broaddus, pulmonologist, Dr Ferris Fattarais.

Dr Carbone explained about a team national research grant they have just applied for that has to involve 4 different projects including clinicians and scientist on each project, Meso has never previously received such a large team grant and whilst they are hopeful this year they have to be realistic that the economy is not great currently which may limit success. He reassured the audience that researchers and clinicians are working together and they are not competing with each other but competing against other cancers to get funding.
Dr Andrew Todd described the tissue bank he is director for. The tissue bank has been funded by a National Insulators Union because they recognise that most of their workers who go on to develop meso are treated at smaller local hospitals and any tissue taken as part of their diagnosis has previously been thrown away. The plan is through this insulators tissue bank to now start collecting that tissue. Dr Todd is also now involved in work with Dr Carbone, collecting blood from people previously exposed to asbestos who attend for screening so that their biomarkers can be monitored.

Dr Broaddus explained how new scientists are being mentored and developed in some of their labs. She also explained that funding from the MARF organisation has been critical in getting many scientists working in meso started. MARF provided the funding they needed to get on the research ladder and then be able to apply for larger grants.

Dr Becich explained how a MARF grant coupled with advocacy influenced the funding a large centrally funded federal grant. There was lengthy discussion about how essential advocacy is in terms of influencing funding bodies and government policy. Erica Ruble explained how she and her family have been helped to cope with the loss of their father/husband through their sponsoring of two research grants in the name of their father through the mesothelioma foundation, Erica said they feel really connected with the scientific community and feel they are helping to better the situation for future patients.

All of the clinicians and scientists attending the meeting funded their own transport and hotels fees and Mary explained that they are always eager to attend to mix with patients and MARF supporters. Dr Broaddus said the first time she attended and presented she felt quite unsure about what to expect but now admits to this being her favourite meeting.

Again an hour and half lunch session followed allowing clinicians, scientists, patients and carers to mingle.

The afternoon split into two sessions. In one room Anna McCurdy lead a panel discussion about the MARF mesothelioma community. There were 6 members on the panel, they were either patients or carers and each took it in turns to describe how they came to be in touch with the foundation and they have benefited from being part of the community.

The final session of the afternoon was presented my Erica Ruble about fundraising. Erica lost her dad to mesothelioma; she is an attorney with a young family but has become so determined to raise funds for mesothelioma research that she now works two days a week for the foundation leading on fundraising. Erica and her family have funded two research grants in her father’s name at $100 000 and is well on her way to funding a third. Shelly Kozicki then explained how she has raised $250 000 in the name of her husband who died in 2009 after an 11 year battle with
mesothelioma. Shelly and Erica proceeded to encourage all present to fundraise and signpost people to the foundation.

Concurrently a closed scientific session was held for all the scientists and clinicians in the room that repeated all the previously presented data but in more detail with opportunities for discussion.

The evening reception commenced at 6pm with dinner at 7pm. A number of awards and grants were announced throughout dinner. The excellent Meso Fighters, a band convened of patients, carers, bereaved and doctors (Dr Lee Krug) entertained before and after dinner playing though provoking inspiring songs.