

Mesothelioma Applied Research Foundation

www.curemeso.org

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Descriptors Board

Board Members are selected to represent the stakeholders in mesothelioma

Three attributes are considered of high importance time, talent and capacity to advance the mission

Advocates bring additional talent to board in addition to their personal relationship to the disease

Scientific Advisory Board

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Challenges in MPM Clinical Trials

**Mesothelioma is a rare disease, and
as a result.....**

- **Large trials take a long time to complete**
- **Less research funding available so fewer investigators interested**
- **Less interest by pharma companies due to low profitability**

But there is a need...

- **Mesothelioma has an extremely high rate of relapse after surgical resection**
- **Pemetrexed + cisplatin is the only FDA-approved chemotherapy regimen for advanced disease**
 - **Improves median survival by 3 months**
 - **Disease ultimately progresses after treatment**
- **Very limited data on the efficacy of second-line therapy**

Approaches for Development of Novel MPM Therapies

- **Adjuvant**: After surgery or combined modality therapy
- **First-line**:
 - Add new agent in combination with pemetrexed / cisplatin
 - Develop new regimen
- **Maintenance**: After treatment with pemetrexed / cisplatin to maintain response
- **Second-line**: At progression after 1st line therapy

The Clinical Trial Process

- Preclinical: Discover new compounds in the laboratory. Assess their efficacy and toxicity in animals.
- Phase I: Administration of new drugs or combinations of drugs to patients to determine safety and proper dose
- Phase II: Use one dose in a select patient population to determine efficacy
- Phase III: Compare new treatment to standard therapy by randomization

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What Needs To Be Done?

1. **Unify the strong voices from patients and their families**
2. **Expand funding opportunities**
3. **Encourage collaboration among investigators**
4. **Increase enrollment on clinical trials**
5. **Develop a patient registry**

The Meso Foundation is helping with all of these needs

1. Unify the strong voices from patients and their families

- Symposium brings community together for education and support
- Lobbying on Capitol Hill for asbestos legislation
- Establishment of Mesothelioma Awareness Day (September 26)

2. Expand funding opportunities

- The Meso Foundation has provided **\$7.6 million** in grants to researchers
 - High level peer review process by the Scientific Advisory Board
- This “seed” money has allowed submission of larger grants to other funding sources
- Solicitation with members in Congress led to grant appropriations through the Department of Defense
 - 4 DOD meso grants, all previously funded by Meso Foundation

Advocacy Efforts

- As a direct result of Foundation's advocacy, the Department of Defense (DoD) has awarded a total of **\$8.8 million**
- to mesothelioma research since 2008

WT-1 Peptide Vaccine Initial Pilot Trial

- WT1 is a tumor suppressor gene highly expressed in mesothelioma
- We developed a vaccine comprised of 4 modified peptides that would induce an immune response against WT1
- We conducted a pilot trial in patients with MPM to show that it was safe and immunogenic

SUPPORTED BY \$100,000 GRANT FROM MESO FOUNDATION

WT-1 Peptide Vaccine Adjuvant Study Design

- Malig Pleural Meso
- WT-1 positive
- 4-12 weeks since completion of multi-modality treatment including surgery
- PS \geq 70%

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Specific Immunotherapy:
WT-1 vaccine / Montanide
+ GM-CSF

Non-specific Immunotherapy:
Montanide + GM-CSF

Primary endpoint: 1-year PFS

Aim to increase from 50% to 70%

N=78 patients (39 per arm)

SUPPORTED BY \$1.5 MILLION GRANT FROM DEPT OF DEFENSE

3. Encourage collaboration among investigators

- Annual Symposium brings researchers together
- Support of the National Mesothelioma Virtual Bank
- Involvement in the SP0RE grant application

4. Increase enrollment on clinical trials

- Meso Foundation provides a resource for patients, and refers patients to appropriate centers for trials
- Future establishment of a mesothelioma clinical trials consortium

Ongoing (or Recently Completed) Large Clinical Trials in Advanced MPM

<u>Drug</u>	<u>Line</u>	<u>Phase</u>	<u>Sponsor</u>
Bevacizumab	1 st with pem/cis	II/III	French Intergroup
CBP 501	1 st with pem/cis	RP II	CanBas
Cediranib	1 st with pem/cis	I/II	SWOG
Everolimus	2 nd or 3 rd	II	SWOG
MORAb-009	1 st with pem/cis	II	Morphotek
NGR-hTNF	Maintenance	RP II	MolMed
Thalidomide	Maintenance	III	Netherlands Cancer Institute
Vorinostat	2 nd or 3 rd	III	Merck
WT-1 vaccine	Adjuvant	RP II	MSKCC

The **Meso Foundation** is the only 501 (c)3 non-profit that:

- **The Meso** Funds leading peer-reviewed research
- Provides complimentary educational and
 - support resources
- Advocates for increased federal funding of
 - mesothelioma research

Conclusions

- Despite many hurdles, advances are being made in the treatment of mesothelioma, but too slowly
- Collaboration across institutions is necessary to more rapidly develop ideas and to complete large studies
- Support from patients and foundations will increase the chance of success