Therapeutic Treatment for Traumatic Brain Injury (TBI)
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Potential for TBI Treatment

- Every 15 seconds in the USA someone suffers a TBI.
- Causes more deaths in men under 35 than all other diseases combined.
- Costs for long term care estimated at $40-50 billion each year.
None of the available medical therapies provide substantial relief from oedema and raised ICP, or at best, they are temporizing in most cases.”


50 compounds in 30 TBI trials over 30 years—all failed. Most recently:

Methylprednisolone (CRASH trial) Failed
Magnesium Sulfate Failed
Dexacannabinol Failed
Tirilizad Failed

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Pseudopregnancy Reduces Edema

Progesterone Reduces Edema in Male and Female Rats

REDUCED EDEMA
Opportunity

- High dose progesterone, i.v.
- Phase II clinical trial completed – therapeutic efficacy demonstrated
- Potential therapeutic markets
  - Traumatic CNS injury
  - Stroke
  - Ophthalmologic diseases

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R & D Status

- Extensive animal model data supporting hypothesis

- Phase II Clinical Trial
  - Double blind, placebo controlled
  - $2.5M NIH funded peer-reviewed project
  - **PI**: Arthur Kellermann, MD, MPH
  - **Project Leader**: David W. Wright, MD

- Phase III Clinical Trial plan submitted
  - NIH funded

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Phase II Study
Subjects

- 100 enrolled (Grady Hospital)
- 71/100 (71%) male
- 72/100 (72%) severe TBI
- 35/100 (35%) African-American
- 58/100 (58%) brought by air EMS
- 76/100 (76%) caused by motor vehicle or motorcycle crashes.
- The others due to falls (6), assault (7), pedestrian struck (3), on the job injuries (3)

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Mortality by Treatment

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Percent dead 100 subjects</th>
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</thead>
<tbody>
<tr>
<td>Progesterone</td>
<td>13.60%</td>
</tr>
<tr>
<td>Placebo</td>
<td>30.40%</td>
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</table>

11 lives saved in Phase II Trial
Disability Rating Scale
Initial GCS = Moderate

(Lower score = better outcome)
Future Directions

- Progesterone already shows *pre-clinical* promise in the treatment of transient and permanent cerebral ischemia.
- May be useful in the treatment of pediatric and geriatric TBI.
- May be useful to reduce edema and complications of cardiac by-pass and vascular surgery.
- Currently being investigated as potential therapy for MS.
First Patent Filed October, 2000

Claims Address:

- Method of treating traumatic central nervous system injury using progesterone
- Method of treating traumatic brain injury using a two level progesterone dosing regime
- Method of treating traumatic central nervous system injury using progesterone where termination of treatment is tapered
- Method of monitoring treatment of traumatic central nervous system injury by monitoring at least one biomarker (tPA, thrombin, neuroserpin or CF-XIII)

US – Provisional and PCT applications

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