Market Exclusivity for Haemophilia Products

HOW TO CONSIDER THE NEW EXTENDED HALF LIFE FACTORS

Jerry S. Powell, MD
Professor of Hematology and Oncology,
Director of the Hemostasis and Thrombosis Center
of University of California at Davis
CALIFORNIA, USA

September 2013
Agenda

• Review progress made in hemophilia
  – And consider why
• Concepts in the clinic
  – Half life of factor
• Extended half life products in clinical trials

“most exciting time in hemophilia in 25 years”

Maybe?
Progress in hemophilia

• Life expectancy in 1960 approx. 20 years
• In 2013, normal life expectancy

• No other genetic disease has had that impressive track record of progress.
• What accounts for this progress?
The half life of Factor VIII in cryoprecipitate is the same as the half life of current Factor VIII products.

40 years without improvement in half life?
Clinical trials in action

It takes a team =
  everyone at every level

Science
  necessary, not sufficient

Enthusiasm
  appreciate subjects on clinical trials

Simplicity = focus on goal
  simple trial design

Regulatory Agencies
  proper understanding

My fear of market exclusivity……
Progress in hemophilia

Key reasons:
1. Science
2. Enthusiastic patients who demand progress
3. Profits to motivate the pharmaceutical companies

Track record of safety:
No patient harmed in 30 years of clinical trials in hemophilia
What to fear in hemophilia in 2013?

Intracranial hemorrhage
occurs approximately 1 in 200 patients per year

Spontaneous bleeding
is a function of time with factor level < 1%

Central venous access devices with associated medical complications

Clearly much more work needs to be done
Goal for treatment of hemophilia

World Federation of Hemophilia, July 2012

“No boy should ever have a factor level of less than 15 %”

Can we achieve this goal now?
Purpose of market exclusivity?

Provide special status to a product to treat a rare disease

- Generally justified as necessary to provide incentive for scientists and pharmaceutical companies to invest in the treatment.
Market for hemophilia

- Projected world wide market for 2016 = $11.4 billion

- Not an orphan drug situation.....

Morningstar Healthcare Observer Analyst Team  January 2013
New Products for hemophilia

1. Factor X, supplement with FVIIa
2. Fusion Fc antibody: VIIa, VIII, IX
3. rFIX-albumin Fusion Protein
   with cleavable activation peptide that releases active FIX
   -perhaps FVIII in the works
4. Pegylated Factor VIII
5. Glycopegylated Factor IX-gp, phase I
6. TFPI inhibitors
7. Anti-sense RNA for antithrombin
8. Human cell line Factor VIII

*After 20 years of recombinant factor products….. now a very exciting area of development*
Concerns with new extended half life products

1. Half life considerations
2. Adverse profiles
3. Inhibitor development
Factor VIII half life

Minimum for surgery

Risk of spontaneous bleeding

Frequency of dosing determined by half life (10 hours)

but individual variation is from 6 hours to 16 hours.
Who can predict the benefit for each individual patient?

- Half life = 6 hours vs 16 hours
- Biological range of extension of half life with FVIII-Fc = 1.2 times to 2.0 times
- RESULT:
  - A range expected from 6 hours x 1.2 = 7.2 hours
  - to 16 hours x 2.0 = 32 hours
Who can predict the benefit for each individual patient?

- Half life = 6 hours vs 16 hours
- Biological range of extension of half life with FVIII-Fc = 1.2 times to 2.0 times
- RESULT =
  - A range expected from 6 hours x 1.2 = 7.2 hours
  - to 16 hours x 2.0 = 32 hours

With several products coming to market, who can predict which product will provide the maximum advantage for each patient?

Market exclusivity may prevent answering this question.
Other questions:

• Several different mechanisms of action
  – Which molecular modification will have different side effects?

• Inhibitor development:
  – Which factor preparation will lead to lower inhibitor formation?
  – And in which genotype/phenotype hemophilia patients?
Typical results of “research”...and unforeseen consequences.

Stay tuned......
Summary hypothesis:

1. Many products in development….. driven by large current and projected market

2. Many unanswered questions about each product

3. Many needs to be resolved for patients with hemophilia

4. Most exciting time in 25 years for hemophilia, perhaps in 40 years

5. Market exclusivity may interfere with clinically addressing these concerns
Why I fear market exclusivity:

“A danger that market exclusivity could potentially create a monopoly rather than allowing market competition that would ensure the widest possible access at the most affordable price.”

Medical and Scientific Advisory Council (MASAC)
Document #208 May 6, 2012