Baricitinib in RA – *What Happened?!!!*

How could safety & dosing issues (Phase II parameters) be reasons for FDA rejection, after conducting four (4) Phase III studies?

April 14, 2017

Baricitinib (Lilly, Incyte) receives an FDA letter, citing safety and dosing concerns, not allowing for approval in its 'current form'.

Conducted 4 Phase III Studies in with ~2000 patients

Strong efficacy data:
- Non-inferior to methotrexate
- Successful vs. Adalimumab
- Better than placebo

December 15, 2016

EU approves barcitinib in RA but notes following, as very common or common:
1. Upper respiratory tract and herpes zoster / simplex infections
2. **Hypercholesterolemia**
3. **ALT (liver enzyme) >3x normal**

Quick literature review

2014 – Phase IIb study shows elevated lipid profile at week 12

2016 – Phase III RA-BEACON study shows elevated ALT and lipids

April 17, 2017

Morgan Stanley's investor note cites two hypotheses for the rejection:
1. Not enough patients tested, compared to Galapagos' filgotinib (~6000)
2. **Lipid levels and liver toxicity may have contributed**

2017 – Phase III RA-BEAM study also points to elevated LDL

Baricitinib has consistently had lipid and liver issues in clinical development…all of which was documented. Baricitinib succeeded in its Phase III objectives, but seems is now being judged for earlier phase parameters. Lilly drops $4B in market cap in one day due to news. US pricing may be higher to re-coup lost sales.

Why did the FDA cite safety/dosing concerns now? Did they make Lilly/Incyte aware earlier? Did Lilly/Incyte not ask the right questions of the FDA, at the right time? Was there a communication gap between one or both parties during Phase II to III transition?