Rethinking Placebos

And what’s RWE have to do with it?

But first, some (very simple) definitions…

Real World Data (RWD)

Data collected outside of the formal clinical trial process (i.e. surveys, registries)

Real World Evidence (RWE)

Conclusions gleaned from RWD

How does RWD/RWE fit into the overall data process?

- **Complementary** to traditionally acquired (clinical trial) data
- Designed to supplement, **not** replace
- Helps researchers see more of “the whole picture” (especially the “patient perspective”)
- Is increasingly being looked at or even required by regulators (i.e. 21st Century Cures Act)
- Is a “work in progress” as standards are still in development

But what does RWD/RWE have to do with placebos?

- Anecdotal information obtained from years of talking to patients (RWD) has led us to believe that placebos have a harmful effect. (hypothesis generation)
- Collecting information on PFS and OS in our registry (RWD) and further analyzing it can provide evidence (RWE) to support that hypothesis.
- Combining this information with that obtained from placebo participants in clinical trials gives a clearer and more complete idea of what may be happening.

The big question: Do placebos harm patients?

Well, let's take a look at the data…

Placebo data from various trials for GIST medications…

including Imatinib, Sunitinib, Regorafenib, Ripretinib, and Pimitespib

From an article in a recent issue of ***LRG Science***

Hey, wait a minute…

What about Avapritinib/Ayvakit?

Not listed, as they did **not** use a placebo
in their D842V trial (the one that **got approved**).

(Therefore, it **is** possible)

Always available at https://liferaftgroup.org/lrg-science/

Summary

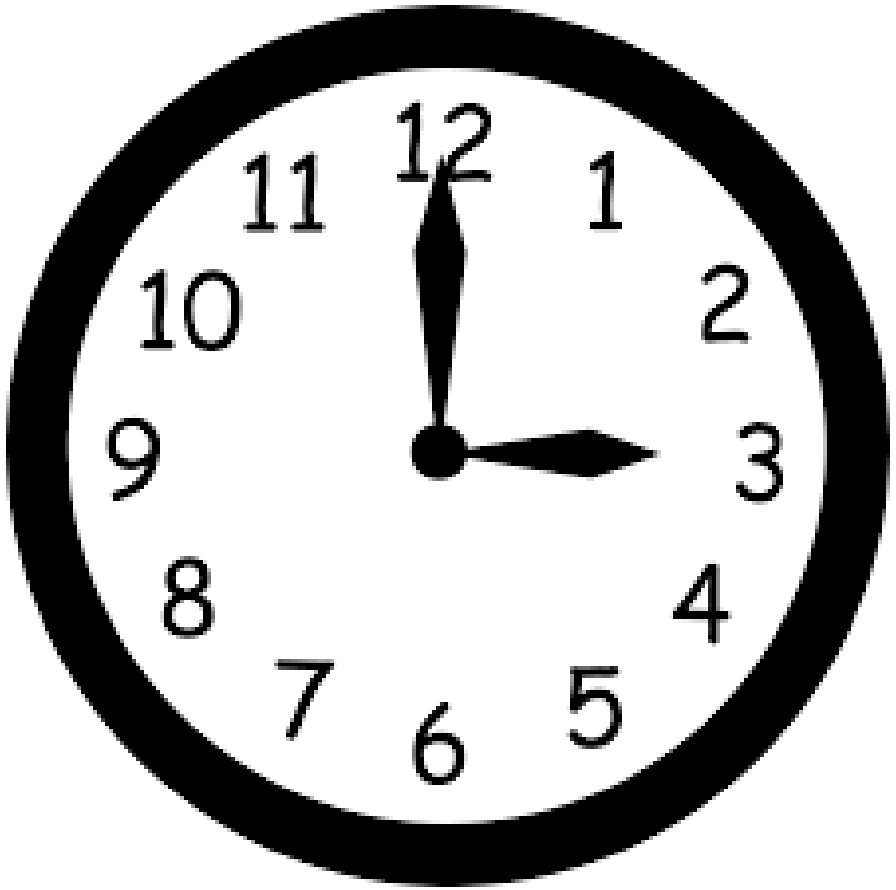
- Placebos in advanced GIST **shorten lives**; this can occur even with crossover designs.
- PFS has become the primary outcome measure in GIST
  - Access to additional treatments and crossover from placebo confound survival as a primary endpoint. As a result, all of the imatinib-resistant GIST registration trials (correctly) consider this a secondary endpoint.
- Placebo arms in multiple trials have extremely similar results
  - 0.9 – 1.4 mo. Median PFS

Summary

- New trial designs are emerging – and RWD/RWE can help
  - Multiple comparison arms with a single, common placebo arm.
  - Synthetic control arms (Cytel)

- It's time for a new trial design in GIST, using common placebo data, from already completed trials, and/or RWE.
  - The remarkable consistency of progression in GIST patients not on a TKI (natural history of the disease) make this design possible.
  - RWD currently exists for GIST and is getting more comprehensive and robust every day.

It’s Time…



For questions….