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 Pimtespib

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....