expedite your drug development.” Woodcock thinks that more such trials are on the way. “That’s where the companies are most interested, and patients are very interested in getting all the way to an approved product that benefits the disease,” she says.

Esserman says that she hopes to eventually graduate combinations to phase 3 within the trial as I-SPY continues to innovate. The US National Institutes of Health awarded a P01 grant to Esserman to adapt the therapeutic course within trial participants (that is, patients within a subgroup who share particular characteristics), such that patients within a trial arm may move to sequences of therapies that hold promise for that subgroup. “We’ve had several conversations with FDA about that modification to I SPY 2—they want to do this kind of thing, but they recognize, as we do, that it’s really a difficult route to drug approval,” said Berry.

Berry thinks that running complex multi-arm trials will require a neutral arbiter with no intellectual-property stake in the middle. For I-SPY 2, it is trial sponsor Quantum Leap Healthcare Collaborative, but government support will probably be critical for the proliferation of such adaptive learning trials. According to Woodcock, the FDA works closely in the planning stages for all the platform consortia. Europe’s Innovative Medicines Initiative (IMI) has also stepped to the fore, supporting the European Prevention of Alzheimer’s Dementia Consortium trial starting in 2015.

Bayesian trials were encouraged in the US under the Prescription Drug User Fee Amendments of 2017 and 21st Century Cures Act in 2016, which created the Complex Innovative Trial Designs Pilot Program at the FDA. Woodcock says that the FDA received several applications from companies interested in developing adaptive Bayesian trials since the program

was launched last year. And in January, Wave Life Science announced that the FDA approved its application for a planned phase 2/3 trial of suvodirsén in patients with Duchenne’s muscular dystrophy amenable to exon 51 skipping; the trial will leverage historical data to decrease the size of its control group.

As adaptive learning trials take root, Woodcock thinks that I-SPY 2’s influence will continue to be felt. “Because it’s been successful, it’s shown people you can evaluate a lot of biomarkers for prediction and also prognosis. You can learn about multiple things at once, rather than just do a single trial about every single intervention. I think it’s showed the field this can be done.” □

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Around the world in a month

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