Q&A

Craig Tendler: Real-world potential

Data from electronic health records and medical-insurance claims can tell researchers how drugs perform outside controlled clinical trials. Craig Tendler, head of oncology clinical development and global medical affairs at pharmaceutical company Janssen, a subsidiary of Johnson & Johnson, spoke to *Nature* about the advantages — and challenges — of using real-world data for drug development and to improve clinical-trial design.

What are the greatest opportunities for real-world data in oncology?
Real-world evidence is never going to replace the gold standard of a randomized controlled trial. It does, however, help drug makers to better understand during development how a drug might perform, by indirectly comparing it with the outcomes that existing drugs achieve in similar groups of people in the real world. After a drug is approved, real-world data can inform safety labelling and be used to identify subgroups of people who are most likely to benefit from the therapy. This helps health-care providers to make the best choices for their patients.

How can this type of data accelerate drug development?
One example is Janssen's development of a fibroblast growth factor receptor (FGFR) inhibitor called erdafitinib (Balversa) for bladder cancer. People with bladder cancer are often treated with immunotherapy drugs called checkpoint inhibitors. We proposed that there is a subgroup of people in that group with FGFR mutations that might not respond as well to these drugs as the overall population, and would be better treated with Balversa.

We looked at the real-world outcomes of people who were treated with checkpoint inhibitors, and found that people who have FGFR mutations don't respond as well to the drugs as do those without the mutations. Real-world data therefore revealed the FGFR mutation to be a predictive biomarker not only for worse outcomes with checkpoint inhibitors, but also potentially improved outcomes with Balversa. These data formed part of our submission to the US Food and Drug Administration (FDA) for Balversa, which was approved last year for people with bladder cancer with FGFR mutations.

Can these data also improve clinical trials?
We see this type of information being useful in setting up studies. When we're starting a clinical trial, selecting the right hospital or clinic to run it is very important. Specifically, the facility should already be administering the type of treatment that will be used as the study's control arm. If it's not, that site will often struggle to enrol enough people. We could use real-world data — say, a site's electronic medical records — to see whether over the past 2 years a facility has been prescribing the treatment in a control group to the type of person who might be eligible for our study.

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In the past, we had to rely on an investigator's recollection of the type of person they see in their clinic. We would take investigators at their word, which was not always reliable — not because they were being deliberately misleading, but because they would often show recency bias, based on who they had seen in the past month. Real-world data allows us to substantiate that the study would fit well with the way that the site works, and reduces the risk — to the pharmaceutical company, but also to the site — of starting recruitment but then not being able to enrol enough people.

Real-word evidence is already used to uncover serious side effects, but how else can it be used post-approval?
We often test drugs in a very homogeneous population that's defined by eligibility criteria in a clinical trial. But once the drug is approved, it will get used in a much more diverse population.

When a drug is first approved, we might not have studied its safety in people with, for example, impaired kidney function, or borderline results of blood-cell counts. So what we can do is start collecting safety data from the electronic medical records. Do people with a kidney impairment have the same side effects as the general trial population, or do they experience new effects? If they do have side effects, can they keep taking the drug for the same amount of time as people in the original study, and still go about their daily activities?

What are the obstacles to realizing the potential of real-world evidence?
I think you still need to have a healthy bit of caution around using the information. We need to make sure that whatever the computer is generating makes sense and is real. So although the initial data collection can be done very efficiently using a form of artificial intelligence called natural-language processing, you still need oncologists to review the data and confirm that what the system is generating is accurate. For example, we might ask the computer to search for any person who had a specific side effect. But when specialists look at the results, they might see that some of the hits the system returned include the right terms, but do not say that the person experienced the side effects.

We also have to make sure that the data collection and analyses are robust. That means not cherry-picking data, but specifying a study protocol and a plan for statistical analysis upfront. This is very important to reduce the level of bias that's inherent in these types of non-controlled indirect comparisons.

Interview by Julian Nowogrodzki
This interview has been edited for length and clarity.