To The Editor: As noted by Brom et al, limited observational studies investigating IgA vasculitis have been reported from Latin America, and these cohorts have thus far focused only on pediatric populations. These aforementioned studies present data similar to that reported by Brom et al, as well as our group, demonstrating a less severe renal outcome among pediatric cases of IgA vasculitis. Although the comparative data between the pediatric and adult groups in the report by Brom et al needs to be considered in the context of the small size of the adult population presented (n=11), these findings remain consistent with other reports, including ours, that adult-onset IgA vasculitis appears to be associated with more frequent renal involvement and a more aggressive course. As mentioned by Brom and colleagues, several genetic polymorphisms have been suggested to be associated with the severity of IgA vasculitis; however, the majority of these studies have used genetic analysis from pediatric populations with limited numbers of adult participants. As such, it is unknown whether there is a genetic variance between adult and pediatric-onset IgA vasculitis that may account for the difference in disease presentation and outcome. Because of the retrospective nature of our report, we were not able to assess genetic variance between our adult and pediatric cohorts. This remains an important area of investigation going forward and a call for prospective genetic analysis among patients with adult-onset IgA vasculitis is warranted.

Matthew Koster, MD
Michel Villatoro-Villar, MD, MS
Department of Rheumatology
Mayo Clinic
Rochester, MN

In Reply, IgA Vasculitis (Henoch-Schönlein Purpura) in Argentina: Comparison Between Pediatric and Adult Population

To The Editor: Despite the limitations of a retrospective study, we believe that our research contributes to the understanding of IgA vasculitis by demonstrating the more aggressive clinical phenotype of the disease in adults for the first time in the Latin American population.

Martin Brom, MD
Ignacio J. Gandino, MD
Marina Scolnik, MD
Rheumatology Unit
Hospital Italiano de Buenos Aires
Ciudad Autónoma de Buenos Aires, Argentina

Potential Competing Interests: The authors report no competing interests.


Potential Competing Interests: The authors report no competing interests.


Oncology Drug Advisory Committee Recommendations and the US Food and Drug Administration’s Actions

To The Editor: Recently, the US Food and Drug Administration (FDA) approved selinexor for patients with multiple myeloma, overruling the final vote of the Oncology Drug Advisory Committee (ODAC). Several oncologists voiced criticism of this approval, citing marginal objective response rate, largely partial response, and considerable toxicity.

The FDA requests ODAC recommendations at their discretion, often when additional guidance could be helpful (e.g., questionable risk/benefit ratio). With the recent discordant decision, we sought to investigate how often the FDA adheres to and overrules ODAC recommendations.

We reviewed ODAC meetings from January 1, 2006, through
May 31, 2019, for decisions involving drugs requesting marketing approval. We excluded decisions regarding biosimilars, generics, and meetings involving the Pediatric Oncology Subcommittee. We abstracted meeting dates, the drug under consideration, the manufacturer, the condition for which the drug was being considered, the ODAC question being voted on and voting outcomes (quantitative and qualitative), the FDA approval outcomes, and date of approval, if applicable. We used publicly available data, which did not require institutional review board approval. Others have looked broadly at safety and efficacy decisions, but ours is the first to focus on oncology drug approvals.3

Of the 61 ODAC decisions, 30 were in favor of approval (all FDA approved), 30 were against (7 approved), and there was 1 tie (FDA approved).

There were seven (11.5%) instances when the FDA approved a drug after ODAC voted against it; 1 instance where ODAC was evenly split on their decision and the FDA approved a drug; and 0 instances when the FDA rejected a drug approval after ODAC’s recommendation to approve. Twenty-five were unanimous votes either in favor (n=16) or against (n=9) an approval (Figure).

Among drugs with discordant conclusions, the percentage of ODAC votes in favor were: bevacizumab (breast cancer) — 44.4%; selinexor (multiple myeloma) — 38.5%; panobinostat (multiple myeloma) — 28.6%; and gemicatibine (ovarian cancer) — 16.7%; olaparib (ovarian cancer) — 15.4%; olomacetaxine mepsesuccinate (chronic myeloid leukemia) — 12.5%; and erlotinib (non—small cell lung cancer) — 7.7%.

We found that the FDA and ODAC reach divergent conclusions in 11.5% of decisions, with a wide range of response and risks from drugs in question. One noted example is that of bevacizumab in metastatic breast cancer. Despite a negative vote by the ODAC, the FDA granted bevacizumab accelerated approval in 2008.7 Less than 4 years later, the agency revoked marketing authorization after multiple randomized trials failed to show a survival benefit.5

We also found that ODAC often votes strongly for or against approval. For ODAC decisions in which the FDA voted against the decision, the agreement among votes varied, but most instances show a largely unified vote against a drug (four of the seven decisions with fewer than 20% of votes in favor of the drug). Discordant decisions between the FDA and ODAC are surprising given the high degree of consensus among voting ODAC members.

In conclusion, our analysis suggests the FDA often approves drugs contrary to ODAC recommendations, sometimes because additional data are provided to the FDA, but there is no indication the agency denies approval despite favorable ODAC views.

Alyson Haslam, PhD
Jennifer Gill, MS
Knight Cancer Institute
Oregon Health & Science University
Portland, OR

Vinay Prasad, MD, MPH
Division of Hematology Oncology
Knight Cancer Institute
Oregon Health & Science University
Portland, OR

Potential Competing Interests: Dr Prasad reports receiving royalties from his book Ending Medical Reversal; that his work is funded by the Laura and John Arnold Foundation; that he has received honoraria for grand rounds/lectures from several universities, medical centers, and professional societies and payments for contributions to Medscape; Dr Prasad hosts the podcast Plenary Session, which has Patreon backers. Dr Haslam and Ms Gill have no disclosures to report.

1. @VincentRK. “Don’t hate the player; hate the game.” Selinexor (Xpovio) approval & pricing highlights what’s wrong with our system. 1) Incorrect approval decision by FDA 2) Outrageous pricing of $22000/month I doubt I’ll recommend or use this drug, till I see data from RCTsThread 1/. https://twitter.com/VincentRK/status/114758640171998032. Accessed July 6, 2019.

2. @diberri. Some initial thoughts on the selinexor approval; it’s great that FDA has identified pentaxifratory myeloma as an unmet need. In theory, it’s...


