Paper PP15

Roadmap to an ODAC: the journey to and through an FDA Oncologic Drug Advisory Committee as a study lead programmer

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ABSTRACT

An FDA ODAC can be a daunting proposition for any programming team, especially when they are unexpected and at short notice. As a study lead programmer who is responsible for the day-to-day programming activities on a study, how is it possible to manage the programming of an enormous influx of additional adhoc output requests to support an ODAC, whilst continuing to make sure everything else at a study level runs smoothly?

In this poster, I will walk through the journey of planning and preparing a programming team to execute and fulfill the requirements needed prior to an FDA ODAC, what efficiencies we built into the process, as well as what lessons we learned. Additionally, I will share my experience of what is required of a programmer on the day of the ODAC itself and being prepared to provide programmatic outputs at the drop of the hat.

INTRODUCTION

This paper and poster focus on a perioperative Non-small Cell Lung Cancer (NSCLC) trial within AstraZeneca. Perioperative meaning that the trial contains a surgery element, with a patient being treated both pre- and post-surgery. Patients are randomised to either Durvalumab plus Standard of Care, or Placebo plus Standard of Care, and they receive this as their neoadjuvant (pre-surgery) treatment for 4 cycles. Then all eligible patients across both arms undergo surgery, before receiving 12 cycles of their randomised adjuvant (post-surgery) treatment.

In the first half of 2023, the trial met both of its primary endpoints, Pathological Complete Response (pCR) and Event Free Survival (EFS) in its first interim analysis. We subsequently submitted to health authorities, including the FDA in July 2023. Following a minimal amount of information requests from the FDA during the time from submission to March 2024, our expectation was that we would start labelling discussions in April, followed by our PDUFA date in May 2024. The study already had a pre-planned second interim analysis to assess our secondary endpoints of Disease Free Survival (DFS) and Overall Survival (OS) which was due to follow the PDUFA date and readout in June 2024.

In early April 2024, we were informed by the FDA that they wanted to hold an Oncologic Drug Advisory Committee (ODAC) in July 2024 to address some concerns they had about our submission. Their main concerns were with the perioperative design of the trial, and if an additional trial was needed to assess the contribution of phases in the study. Additionally, a formal vote was needed on whether future new perioperative trial designs for NSCLC should contain an adequate within trial assessment of contribution of treatment phase.

PLANNING AND RESOURCING

Preparation began by mapping out slides to be prepared for any potential questions to be asked by the FDA during the ODAC. For every slide, there were multiple adhoc requests required to be produced by the statistics and programming team. There was the additional complexity of providing outputs across multiple data cuts, as well as creating outputs using the second interim analysis data cut from June, in time for the ODAC meeting the following month.

This led to a crunch in the timelines, which coincided with a shortage of resource, as highlighted in the poster. Mapping out resource for this period proved challenging and we leveraged programming resource from other teams. It led to our day-to-day programming roles being adjusted and geared towards delivering the ODAC outputs as a priority, whilst still making sure the quality control for our second interim analysis deliverable from the vendor wasn't neglected.

PROGRAMMING

The programming of the adhoc requests began in May 2024. The requests would be raised from the cross functional team based on discussions as to what the FDA may require. This team contained representatives from programming, statistics, clinical and patient safety. A tracker was setup to manage, triage and resource these requests by the statistics and programming leads, before the programming and quality control of outputs was performed. Once completed, each adhoc request was delivered back to the cross functional team for review.

Throughout May 2024, the team were able to focus consistently on adhoc output programming. Consistent production and QC assignments meant teams were able to build working relationships with each other. In June during the busy period, the team was split into two sub teams to manage workloads across different activities. We had ODAC output requests, whilst quality control was starting for our second interim analysis deliverable from the vendor. This deliverable then triggered a new wave of ODAC output requests.

Once the second interim analysis deliverables were finalised, we leveraged vendor programming to support additional requests. A decrease in requests during July enabled programming team to work on other ODAC tasks. Three months of solid programming work culminated in 865 IEMTs being produced to support the creation of over 1000 slides for the ODAC meeting. This worked out at one adhoc output being produced every 30 mins on average, every day, for three months. We could now turn our attention to the day of the meeting and the ODAC itself, so the next stage was to hold mock meetings to simulate the meeting on the day.

ODAC MOCK MEETING

In preparation for the ODAC, the team split across three areas, the bull pen, the back room and the programming room. The bull pen was where the speakers and responders would be in the room with the FDA. The back room contained cross functional representatives, including programming, who managed and triaged any requests made during the ODAC. The programming room was where we had programmers and statisticians ready to action any requests for which we didn't already have a slide prepared. We held two mock meetings prior to the ODAC where we could test the communication and workflows between the three rooms, to simulate how a request would be addressed if needed during the ODAC.

This was useful for the team to iron out any problems, and gather some learnings, so that we felt prepared for any requests we got on the day of the ODAC. One of our main learnings was to make sure that we maintained one line of communication between the back room and programming room. During the mock meeting, some team members from the back room were opening other lines of communication, and whilst they had the team's best interests in mind and trying to be helpful, in the programming room we found it to be distracting.

ODAC MEETING

The ODAC took place at the FDA headquarters on the 25th July 2024, where both AstraZeneca and the FDA began with their opening presentations. The question and answer section followed, with a focus on general perioperative trial designs, as opposed to study specifics. This was followed by an open session where pre-registered members of the public, could give their opinions on the trial from their perspectives.

The discussion by the ODAC deemed that the regimen was safe and effective, and another trial shouldn't be needed prior to approval. The ODAC then voted unanimously that perioperative studies should account for contribution of phase for all future NSCLC trial designs. ODAC meetings are streamed live on YouTube and are open to the public. You can find the link to our ODAC in the QR code in my poster.

POST-ODAC

Three weeks later on the 15th August 2024, we achieved FDA approval for our trial… "*FDA approves neoadjuvant/ adjuvant durvalumab for resectable non-small cell lung cancer*".

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