Paper SA03

Oh Dear, Another Crisis? A Programmer's Guide to Surviving and Thriving Through the FDA ODAC

Zach Dorman, AstraZeneca, Devon, United Kingdom

ABSTRACT

You've put in several months of hard work to complete your datasets, TLFs and submission materials, worked through hours of regulatory response, only to now be told that your study is subject to an Oncologic Drug Advisory Committee (ODAC) meeting held by the FDA. Is it time to panic, or time to shine knowing that you've prepared your team for just this eventuality?

In this paper, I will talk through my experiences of going through an ODAC as a programming lead and oversight – from the initial stages of not knowing what to do or expect, right through to the day of the ODAC itself. I hope to demystify the ODAC process, share some successes and lessons learnt, and give you some tools for how to thrive both as an individual and programming function in this pressured environment, should you be lucky enough to be involved in one in the future.

INTRODUCTION

This paper will discuss the process and experiences that the Oncology Programming team at AstraZeneca went through in the summer of 2024, once an ODAC meeting was called by the FDA for a particular study. We will walk through the timeline of the AEGEAN study, which was a Phase 3 study in resectable non-small cell lung cancer (NSCLC), from the point of submission through to the ODAC meeting and post-meeting activities. Whilst the details of the study are important and help introduce the rationale for the ODAC, this paper will focus primarily on our experience of going through preparation and delivery of an ODAC. Specifically, the timeline of the meeting will be discussed, including the additional activities that needed to be performed alongside the ODAC; the specific work that needed to be done in order to prepare for the ODAC and the additional support over and above usual study functions that was required; how the team set themselves up for success through their setup and assignment of work, and the machinations of the meeting itself. Given this is a novel piece of work to be involved in from a Programming functional point of view, some challenges, wins and lessons learned are also to be discussed, with a view to provide some hints and tips to any Programming team who may have to take part in an ODAC in the future.

All information regarding trial details and specifics in this paper were made publicly available at the time of the ODAC.

SETTING THE SCENE

The AEGEAN study was a Phase 3 study ran by AstraZeneca looking at the efficacy and safety of durvalumab in the perioperative setting – perioperative consists of two distinct treatment phases: Neoadjuvant (which consists of treatment prior to an arranged surgery), and Adjuvant (which consists of treatment following an arranged surgery). Patients needed to have resectable non-small cell lung cancer (NSCLC), ranging from Stages 2A to 3B, and have a planned surgery before entering the study, as well as a number of other different criteria to make them eligible for the study. The main endpoints for the study were Pathological Complete Response (pCR) and Event-Free Survival (EFS), an oncology time-to-event endpoint for resectable NSCLC with a similar derivation to progression-free survival. Information relating to the specific study design can be seen in Figure 1. The study met complete enrollment in late 2021 and had a number of interim analyses lined up throughout 2022 and 2023.

TIMELINE OF THE STUDY ANALYSES AND SUBMISSION

Once the study had completed enrollment, an interim analysis of both EFS and pCR data took place in early 2023, which was found to have statistically significant and clinically meaningful results across both endpoints. This allowed us to move forward with submitting the study data to multiple authorities, including the FDA, from July 2023 onwards. The next several months consisted of presenting a technical walkthrough of our package to the FDA, including an in-depth presentation on the various efficacy endpoints and treatment phases included in the study, and responding to various requests for information on a number of different aspects of the submission.

NOTIFICATION OF THE ODAC

In late March 2024, whilst the team were responding to the first round of requests for information as it related to the label, a notification came through from the FDA that an ODAC was being considered to be convened as it related to the open AEGEAN study. Based on the communications provided by the FDA, there were outstanding questions on the contribution of treatment phases both specifically to AEGEAN, and for wider studies. On 2nd April 2024, the AstraZeneca team received formal confirmation from the FDA that an ODAC would be held to discuss the AEGEAN trial, and general issues with perioperative trial designs which do not demonstrate contribution of phase to the overall regimen.

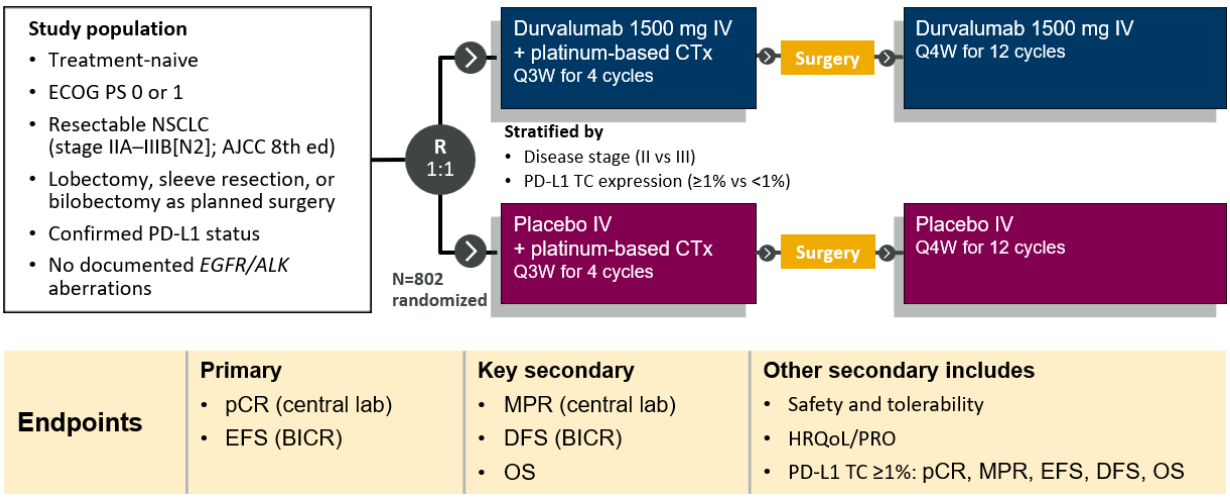

Figure 1: Flow chart of the study design for the AEGEAN study.

WHAT IS AN ODAC?

The Oncologic Drugs Advisory Committee (colloquially known as an ODAC) is a group of experts in the oncology field, that the FDA brings together in order to discuss pertinent topics on ongoing submissions, or to seek expert advice before coming to a decision on whether to approve a particular submission. The committee contains a number of standing members, as well as temporary members who are usually experts in the relevant field of the topic being discussed (such as a particular type of cancer). The committee will be made up of voting members and non-voting members, who are elected to terms sitting on the committee – the voting members are usually doctors in specialized oncology fields, such as immunology, hematology and pediatric oncology, as well as more specialized non-clinical fields such as biostatistics. Other members of the committee include a representative of the pharmaceutical industry, a consumer representative, and a representative for patients.

For each ODAC, there are usually a set of questions or topics that the committee discuss and then vote on. The results of these votes are non-binding, and do not necessarily dictate how the FDA have to move forwards, but are designed to give the FDA further information and viewpoints in which to make a considered decision on how to move forwards with the particular submission and industry topic being discussed. Given that the FDA is a public government body in the USA, they have a commitment to transparency for ODAC meetings, and therefore these are streamed live on YouTube for the general public to watch.

ODAC RUNNING ORDER

The running order for an ODAC is consistent across various meetings that have taken place over the past few years and is the same running order that was received for the ODAC related to the AEGEAN study.

- ***Introduction*** – The committee chair will provide an introduction to all of the committee members sitting on the committee for the particular meeting and read out a statement regarding potential conflicts of interest.
- ***FDA Opening Remarks –*** The FDA will make some opening remarks about why the ODAC has been convened, and their rationale and position for requiring an open public discussion on the topic.
- ***Applicant Presentations*** – This allows the sponsor to present and set out their position on the topics facing their study, or scientific question, that the ODAC intends to discuss.
- ***FDA Presentations –*** The FDA will then provide their presentation on the same topics and questions, providing their viewpoint on the relevant questions for the ODAC to consider in later parts of the meeting.
- ***Clarifying Questions*** - Once both the FDA and the sponsor have provided their presentations, each of the committee members can then ask clarifying questions to either party to gain more understanding of their presentations, and to get further insights that can guide their voting or their discussion later in the meeting.
- ***Open Public Hearing –*** Once all questions have been asked of the sponsor and the FDA, the open public hearing gives members of the public a chance to comment and provide their views on whether the application should be approved, or have a particular viewpoint on the scientific question being posed. Examples of this could include a patient cancer survivor explaining how a particular drug has kept them alive and on the road to recovery, or a public health group explaining the long-term pros and cons of a particular drug coming to market.
- ***Discussion and Vote on Questions to the Committee –*** Once all applicant, FDA and public comments and opinions have been shared, the committee will discuss and vote on the questions that have been put to the ODAC. This will either take the form of a roundtable discussion where members of the committee will be asked to put forwards their opinion on what has been presented to them, or they will vote using their keypads, and the results of the vote will appear on screen to all viewers of the meeting.

QUESTIONS FOR THE AEGEAN ODAC

Following on from the notification of the ODAC, the FDA provided the AstraZeneca team with some draft question wording for what was intended to be discussed at the meeting. After some discussions between the FDA and our internal teams, the final wording of the questions was released prior to the meeting.

There were two questions that formed part of the ODAC that we were involved in. The first question related specifically to the AEGEAN study and the questioning of the perioperative trial design, and wanted the committee to discuss whether there was a need for another trial to be conducted that could separate the neoadjuvant and adjuvant phase contribution, prior to approval of the study. This question did not have a formal vote attached to it – the expectation for the ODAC members would be to discuss this, but the FDA did not go as far as to request the ODAC perform a vote on the topic.
The second question was not related to the AEGEAN study specifically but was more to answer the question regarding perioperative study trial designs, and whether it should be mandated for all study designs moving forwards that the contribution of each treatment phase should be taken into account and be able to be measured via within-trial assessments. Unlike the question specific to AEGEAN, the FDA had asked the ODAC to vote on this particular question, meaning that there would be a Yes/No response for each voting committee member to give at the end of the discussion.

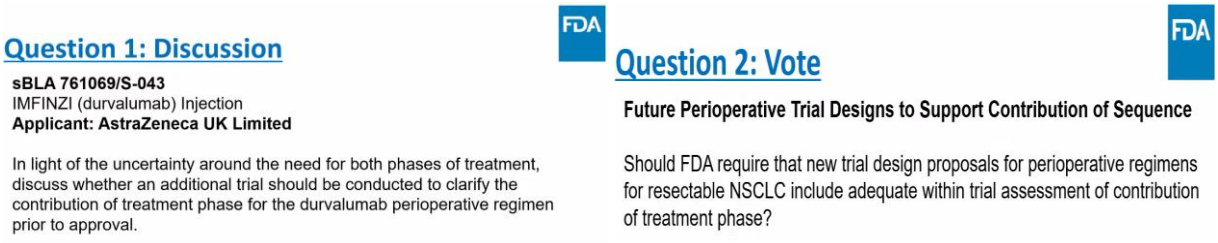

Figure 2: Excerpts from the question list disseminated by the FDA prior to the ODAC.

PLANNING AND PREPARATION FOR THE ODAC

Now that the FDA had confirmed that the ODAC was going to be announced and that we had a date to work towards, it was important that the planning steps started to take place – given that nobody in our programming team had ever worked on an ODAC before, it was quite daunting to know where to start. Luckily, another group at AstraZeneca had undergone an ODAC over the past couple of years and were able to give us a few points in the right direction to make a start. However, given the specificity of the ODAC for this study, it was important to have the right support in place to help us as both a cross-functional and programming team to provide the best support.

EXTERNAL PLANNING SUPPORT

Given the lack of knowledge on how to prepare for an ODAC, our team needed some expert outside guidance in order to start the planning activities and development of the presentation. An outside regulatory consulting group were brought in to help the team navigate the journey up to and including the day of the ODAC. They provided a number of different services to the AZ team, such as working on the slide deck that was going to be presented, and preparing back-up slides in the event that there were questions that did not get answered by the main presentation; coaching the speakers of the presentation to deliver the information in a way that would land the main points with members of the committee; facilitating practice runs and mock meetings, to ensure all members of the team were fully prepared going into the ODAC itself, as well as pulling together all information to create a coherent strategy.

As someone from Programming, who doesn't usually become involved in the high-level strategy of regulatory events, it was fascinating to watch senior and executive members of our cross-functional team engage in this type of strategy, as well as learn from how these executive minds think and approach problems.

AZ OBJECTIVE AND PRESENTATION STRUCTURE

As the planning started to take place for what needed to be presented, a general overview of the topics that AstraZeneca needed to cover became clear, as well as a proposed structure for the presentation. As a result, the presentation that AZ intended to give at the meeting fell into five clear topics. Firstly, an overview of the disease background was to be provided, to give clarity as to why the AEGEAN trial was necessary in the NSCLC space. The presentation followed on to talk about the clinical outcomes of the study, both from an efficacy and safety perspective. Given the discussions were around internal presentations of the results, the senior clinical and patient representatives on the AZ team delivered these sections. It was also determined that a clinical perspective section was required, given the questions posed by the FDA surrounded the topic of additional trials and contribution of phases. Finally, closing remarks and the AZ outlook for further trials in this space was provided by a senior member of the AZ team. For disease background and clinical perspective, outside speakers were brought in, who had further knowledge and information to provide over and above the AZ study team.
The objectives of the presentation (and the basis for all further planning) was to make clear to the ODAC members

that AEGEAN was a positive study, that it helped to address an unmet need in patients with resectable NSCLC, and that steps had been taken to try and address the concerns that the FDA had in their non-specific study question, to support the industry and patient outcomes more generally.

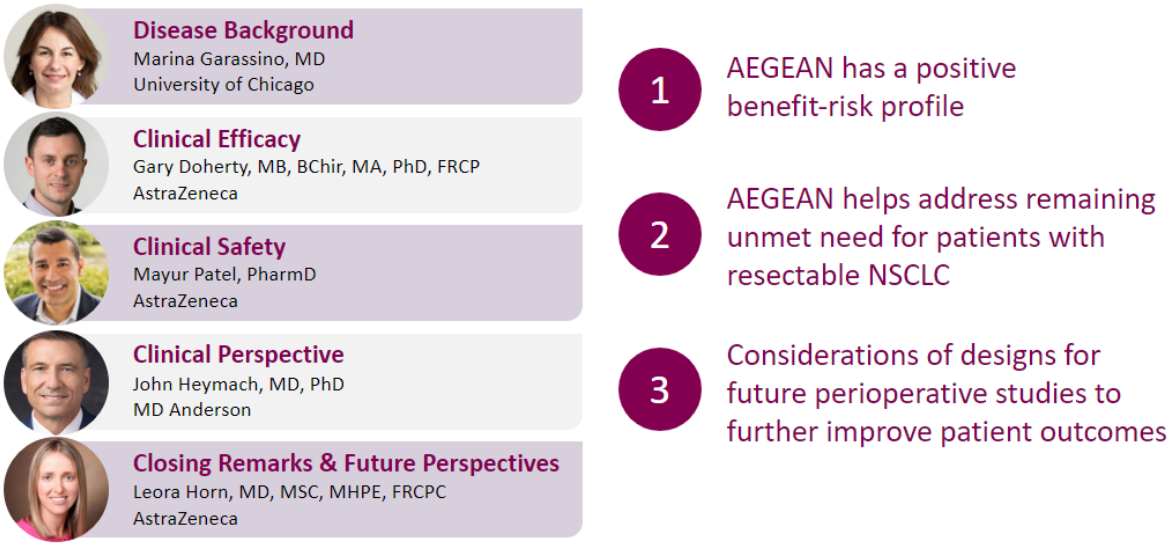

Figure 3: The description of the AZ presentation and objectives, as shared in the ODAC presentation on July 25, 2024.

THE ROLE OF THE PROGRAMMING TEAM IN THE PLANNING

Now that the wider team had a framework of how they wanted to build the presentation, the programming team and I were still not clear where our role started. However, it soon became clear that we had a large amount of work to do to help the team prepare the slide deck and associated materials ready for presenting. This fell into three main categories:

- **Q&A:** As well as the main slide deck that needed to be produced, a large part of the planning that took place revolved around the potential questions we might get from both the FDA and the ODAC members. Therefore, a large exercise was undertaken to think about the types of questions that the team might end up receiving, and this activity resulted in large numbers of questions being grouped into certain categories, such as disease background, study design, safety, benefit/risk etc. The role of myself as the programming representative was to inform teams of whether we had outputs or datasets already available that could start to answer some of these questions (and could therefore be moved directly onto back-up slides), or whether this required a new output to be programmed to answer the question. As the questions started to be fleshed out and developed, this formed the start of a list of ad hoc outputs that I had to assign to my programmer to start working on.
- **Managing complexity of asks:** Although the objectives for the presentation seemed simple, trying to plan out the work needed was anything but that. Given the complexity of the study, with its different treatment phases and endpoints, we had multiple data cuts that could be used to answer a question (this included an initial interim analysis of pCR data, the main interim analysis of pCR and EFS data, as well as a 2nd interim analysis of EFS and OS data that was due to take place during the ODAC preparation periods). As a result, it was a full-time job to understand the nature of the slide or question that the team wanted to answer and work out which data cut would be best placed in order to answer the question. Given that a number of questions revolved around showing impact of different treatment phases, we often had to create multiple versions of the same output, based on either a neoadjuvant or adjuvant treatment phase (this was especially critical for the safety outputs, where the split by treatment phase was crucial to understanding the safety portion of adjuvant treatment).
- **Subteam attendance:** Given the scale of the preparation for the ODAC, it was determined at the initial planning sessions that not every individual would be able to be involved in every aspect of the presentation. Therefore, it was decided to split the teams down into several subteams – these included a Safety, Efficacy and Study Design team, in order to discuss and develop strategy for the various objectives of our presentation. As the ODAC lead, I sat on both the Safety and Efficacy subteams, and my role was to explain whether certain suggestions were possible with the data we had, share if we had outputs that may help answer or contribute to what was being built, and take note of outputs or requests to add to our increasing list of ad hoc outputs that we needed to produce. My role was also to push back on any suggestions that might take more time than we had, and so I had to learn and expand on my stakeholder management techniques to be seen as a reliable and stable stakeholder in these planning meetings.

EXECUTING AD HOC WORK

As we had now started to build a comprehensive list of ad hoc outputs for the ODAC, we needed to come up with a way of managing the resource that needed to go into this work. At first, we thought that the best way to work on the ad hoc outputs that were coming through was to use the existing study teams (as there were two studies within AZ that were needed to contribute data for ad hoc questions), as they would be best placed to understand the data. However, we also had to contend with the fact that both studies had study-level analyses reading out during the ODAC preparation process – the second interim analysis for AEGEAN, as well as the final analysis for the 2nd study being considered. Although both studies were outsourced to vendor biometrics teams, they still required a number of QA resources to ensure the deliverables were correct and to high quality. As part of the planning, I also had to remember that the FDA was not the only authority we were interacting with – we had other requests from other health authorities.

With all of this in mind, I then had to estimate the number of resources required to cover all of the work required across the studies. Once done, we created a line chart to cross-examine the amount of demand we had with the ODAC requirements filtered in, against the amount of supply that our original teams had. The results of this can be seen in Figure 4:

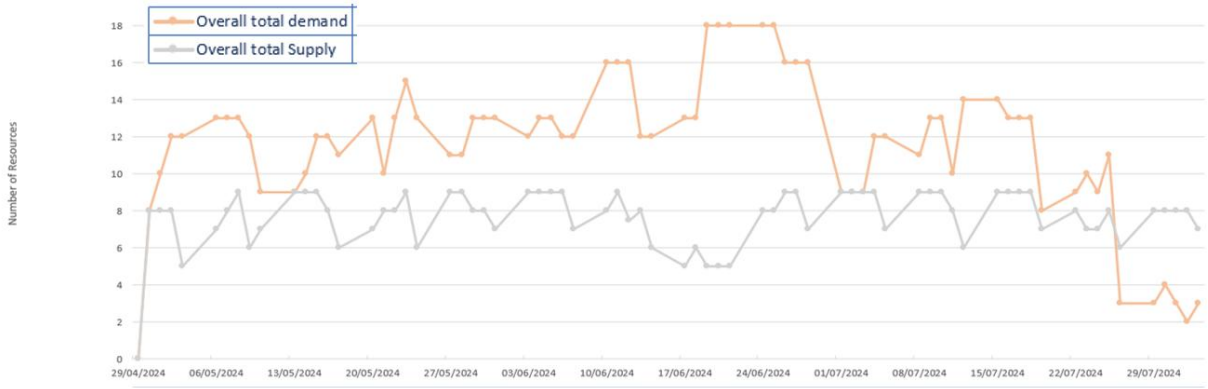

Figure 4: Line chart of overall total demand against overall total supply for the AstraZeneca programming team responsible for the AEGEAN ODAC.

From this, we saw that there was a peak period of work from the middle of May to the beginning of July that we had to navigate, either by stripping back on non-essential activities, or by bringing in additional resources. We ultimately chose a middle path – bringing in some resources to help with the essential ODAC and study related items, as well as challenging wider team members on what was critical for the ODAC, as well as challenging our own plans for the scope of QA we were performing on study deliverables. We also created 3 distinct teams from this point onwards – 2 study teams to manage individual study-level deliverables, and an ad hoc ODAC team, responsible solely for the programming of ad hoc outputs. Each team had a lead, who reported into me from a project perspective to make final decisions on prioritization and resource.

Based on this resource projection, we then produced a plan of action for how to tackle the work coming through. As study work was less of a factor in May, we decided to try and get ahead as much as possible with the programming of outputs, proactively chasing other functions to find out what they may want in the future, as well as what was being discussed right now. We were able to assign production and QC programmers to work on specific sides and, by having additional members during the quiet periods of the project timeline, could build up a bigger base of programmers working on either side to allow us to move resources around as needed later in the project. In order to keep delegation of work more organized, an ad hoc programming tracker was created, for which the programming leads could add new outputs into after discussions with various functional leads. This open tracker made sure that we were not missing potential outputs that had been requested.

During the busy periods in June and July, we also had to deal with unexpected consequences because of the study readouts and additional regulatory interaction. Requests for information from another health authority meant that we had to divert resources from some of the study-level QA work to ensure we were not missing any critical piece of work. Given that June and July are also busy times from an annual leave perspective, we had to manage annual leave periods of key personnel, including two of the leads for our programming subteams. In addition, stakeholders were getting more agitated for outputs relating to their priority, which meant further stakeholder management in my role. Despite these challenges, we were able to manage workload and keep delivering ad hoc outputs. We also took proactive steps to ringfence our ODAC resource as appropriate from additional requests. One example of this was additional requests from the study team following one of the readouts – we were able to successfully push back on this by highlighting the risk that additional activity would have on the externally-facing ODAC presentation, and also take mitigating steps by asking our Biometrics vendor to handle some of the additional, non-critical work, to allow our team to focus primarily on the fast-paced ODAC work.

As the ODAC came closer and we moved into July, the bulk of the study readout work had been completed, which meant we were able to finalize the remaining ODAC ad hoc outputs and dedicate more time to discussing remaining issues with the cross-functional team. As the slide deck started to be finalized as well, we noticed a significant drop off in new requests, which meant we could prioritize other ODAC tasks, such as performing QA of slides before they were finalized and ready for presentation. As a result of the solid programming work from May to July, the ODAC programming team produced 865 ad hoc tables and figures, which were produced in order to support over 1000 slides that were kept in back-up for the presentation.

MOCK MEETINGS AND PREPARATION

As the ODAC process continued in the lead-up to the meeting itself, there were some big milestones that needed to be achieved on our journey. Central to this was the briefing document, which spelt out the AZ position in responses to the FDA's concerns and questions that were being posed to the ODAC, and the mock meetings that were arranged in order to evaluate the team's presentation and ability to respond to questions. Both of these points lead to a spike of requests for ad hoc outputs, both in order to develop material to include in official documentation, and also as a result of late-breaking organization from other functions to prepare what they needed for the mock meeting. There were two mock meetings (one approx. 6 weeks before the ODAC, and another 2 weeks before), both of which had independent panels acting as ODAC members, to then provide feedback on how the presentation was going.
Programming had an important role to play in the mock meetings, as this gave us the first chance to test out how we would react if we were asked to produce something in the meeting itself – perhaps to a question that we had not anticipated. The setup of the team and lessons from that will be discussed in more detail later on in the paper, but as a Biometrics team, we were responsible for dialing into the meeting and listening for any prompts or questions that may mean we need to start programming the answer, and then liaising with the team in the meeting room to pass back the answer for the speaker to show in real time during the course of the meeting.

PROGRAMMING TEAM SETUP FOR STUDY AND AD HOC ACTIVITIES

As touched on in earlier sections of this paper, we had to ensure that the programming team was set up in such a way that allowed us to effectively assign resources to key pieces of work and deliver both to time and quality in a high-pressured situation that continued for several months. As a programming oversight, the planning and setup of the team had multiple facets – setting up the team to program on a day-to-day basis whilst juggling study and ad hoc outputs, as well as thinking about the best way of building a team that could help the wider AZ team during the critical ODAC milestones, and actually be involved in the execution of the meeting on the day.

At AstraZeneca, the programming leadership on a study usually consists of a Global Product Programmer (GPP), a Study Lead Programmer (SLP) and a Back-Up Study Lead Programmer. To provide context to the usual roles and responsibilities first, the GPP is responsible for one or more studies in a programming portfolio and is often advising or providing oversight to the studies (such as standard requests, stakeholder management etc.), as opposed to performing hands-on work. The Study Lead Programmer is responsible for the day-to-day management of a particular study; resourcing and completing the work, managing the workload of the support programmers, and liaising with study-level colleagues across different functions. They are supported by the back up study lead programmer, who is usually more in a hands-on role and providing the technical support and knowledge to complete the relevant programming.

Due to the unique nature of the ODAC, we had to review and look again at the differing roles and responsibilities for each of these positions, to see how they would best fit in the construct of achieving a successful ODAC outcome. As the GPP for the AEGEAN study, it fell to me to lead the discussion about how best we organize. After said discussion, we decided to rearrange the roles and responsibilities of each role on the AEGEAN study as follows:

- ***Global Product Programmer***: Instead of the hands-off, oversight role that the GPP normally plays, it was decided that the GPP would play an active role in the management of the ad hoc outputs that were provided for the ODAC. This meant being responsible for the management and triage of the various ad hoc requests that were coming in from different functions and making sure they were being resourced and worked on by the appropriate people – taking on this task meant that other programmers were freed up to perform the actual programming work. As well as this activity, the GPP maintained active oversight of both the AEGEAN study, and other relevant study in the portfolio that was contributing to the ODAC**.**
- ***Study Lead Programmer*****:** The study lead programmer was now freed up from the resourcing and management of the work, as this had been taken on by the GPP. As a result, the study lead programmer became the technical point of contact for the programmers assigned to ad hoc output production, to support with items like where to find programs that could be modified to support ad hoc outputs, or to provide support in interpreting a request.
- ***Backup Study Lead Programmer:*** As the study lead programmer had now stepped into the ODAC ad hoc work, it meant there was a gap in leading the day-to-day study work that was still required. As the back-up had experience leading tasks on AEGEAN, we decided to move the back-up into the study lead role for the duration of the ODAC project. This meant that we still had someone who was well versed in the study leading the relevant activities, whilst allowing our lead programmer to get more involved in a technical lead role for the ODAC and ensuring high quality across all deliverables.

As well as the lead assignments, there were a large group of support programmers assigned to the portfolio in general, to help support the various studies and the ODAC interactions – at its height, we had 11 support programmers. The overarching plan was to assign support programmers to both individual studies and the ODAC, so they only needed to focus on one area of the project. However, as time went on and our plans fell mercy to events along the ODAC journey, we had to be flexible with assigning programmers to the areas of most need (which is mostly on the ad hoc output side). Fortunately, getting the programmers involved with this early as the ODAC preparation got up and running, allowed us to be effective and efficient during the busy periods, as most of the programmers were able to slot in and support straight away.

TEAM SETUP FOR THE ODAC MEETING

As well as the programming work in the lead-up to the ODAC, Programming was required to provide support to the actual team composition of the ODAC meeting, and to take part in both the mock meetings, rehearsals and the main meeting itself. Programming was one function in what become a cross-functional collaboration across multiple sites and time zones to present the materials in the ODAC. The next section of the paper will explain the three major teams that helped to deliver on the day of the ODAC, and their responsibilities leading up to the event:

IN THE ROOM AT THE FDA

Our main team were a group of individuals that were sitting in the room at the FDA whilst the meeting was going ahead. For the most part, these were senior members of the AZ team, and those individuals who were generally in charge of the strategy we were implementing for the meeting. There were three main roles:

- ***Speakers:*** These were the team members who were responsible for presenting AZ's pre-prepared remarks on our core presentation. As seen in the presentation order earlier in the paper, there were 5 individuals who were talking on the core presentation. The lead presenter (the VP of Clinical Development) also introduced any other person who came up to the podium to talk on behalf of AstraZeneca.
- ***Responders:*** As well as the main speakers for the core presentation, there were also many people who were designated as "responders" – these individuals did not have a role in talking to the core slide deck, but were there to respond should there be any questions from the ODAC members in their field of expertise. Functions that fell into this category included Statistics, Regulatory, PRO and Translational Medicine, amongst others.
- ***Slide Callers:*** These were a group of study team members who were responsible for bringing up slides for the speakers or responders to talk to, that were not on their core presentation. The slide callers had to have a complete knowledge of their section of entire slide deck, so they could bring up slides quickly and in response to the questions being asked by the committee in real time. The slide callers were often the next most senior team member of the study, and would often cover multiple areas, so as not to have too many people in the room. As an example of this, our Global Product Statistician was the slide caller for both the Statistics and Clinical Efficacy sections of the deck.

The team in the room played a critical role in all mock meetings, so they could practice their presentations and Q&A rehearsals before the day.

BEHIND THE SCENES

This team was a group of cross-functional representatives from the key functions that were contributing to the ODAC, such as Statistics, Patient Safety, Clinical and PRO. This team were sequestered in a side room, away from the main room in which the ODAC was situated and watched a live stream of the meeting via a secure link. The role of this team was to listen to any requests for information coming from the ODAC, and triage as to whether the information was already in a slide deck, or whether a response needed to be developed and then communicated back to the team in the ODAC room (there was a communication line via IM between the teams and team members, and people in the ODAC room were able to join their colleagues during scheduled breaks to receive responses in person).
There were three critical roles behind the scenes:

- ***Room Manager***: This individual was to manage the members of the team and was ultimately responsible for the content and information that went back to the team in the ODAC room as a response. This role became more defined after our mock meetings, to ensure there was one voice speaking for all of the team.
- ***Scribe***: This person was tasked with writing down what was happening in the ODAC meeting room, so that there was a record of what was going on. The scribe role becomes really influential when the team feel that a request was made that they need to action, as they are able to refer back to the scribe notes to see exactly what was asked (given the intricacies of the study, a question could take different meaning depending on slight changes in wording), and make sure that the correct instructions and information are given onto the relevant parties.
- ***Biometrics Room Link:*** The Biometrics room link was the Programming Team Lead for the study, and their primary role was to liaise with the Biometrics Room if it is felt that programming is required to answer a question that the current materials are unable to. There was a muted, open phone line between the room at the FDA and Biometrics room throughout the ODAC meeting, that the point people between the two rooms could use to communicate as necessary.

This additional team were available for rehearsals and were activated during our rehearsals. Learnings from this are featured in later sections of the paper.

BIOMETRICS TEAM

A biometrics team (for which I was the lead) were co-located for the week of the ODAC meeting, and were the stats and programming team responsible for producing outputs in real time, should there be a gap in information in the prepared slides and something would then need to be prepared quickly in order to present. In the biometrics room, there were a number of statisticians and programmers so that we were fully prepared for any type of question that might come in – in case of there being multiple requests coming in at the same time, we took the decision to have 5 statisticians and 3 programmers involved, so that we had ample resource to work on multiple items, should that be the case.

Like the team behind the scenes, the biometrics room watched the meeting via a secure link that was transmitted into the meeting room. The biometrics room lead manned the direct link to the team at the FDA, in the event of there needing to be any discussions. There was also a designated stats lead in the biometrics room in case of there needing to be any statistical conversations with their counterparts (given that the leads in the two rooms were both programmers).

THE DAY OF THE ODAC

After all of the preparations, rehearsals, ad hoc programming and slide creation, the ODAC meeting finally came on 25th July 2024 – approximately 3.5 months since we had received the initial notification of the meeting. The meeting started at 9am US EST and followed the running order that has been set out earlier in this paper. The AstraZeneca presentation was delivered without any hiccups, which was testament to the amount of effort and preparation that went into the slide deck and coaching of the speakers. As we moved onto the Q&A portion of the meeting, we were all prepared for our teams to be enacted, especially after hearing both presentations together, and the clear discrepancy around how important the contribution of phase was when it came to approving the AEGEAN regimen. However, we were all surprised to see the conversation move very quickly onto discussing the perioperative trial designs, how to best define those, and why that was never an option for AEGEAN, as opposed to discussing the specifics of our study. The Q&A never really got back to the AEGEAN specifics before the lunch break, and we were then straight into the Open Public Hearing.

It was fascinating to hear the various different members of the public who contributed to the discussion – ranging from doctors specializing in thoracic oncology, members working on behalf of the National Centre for Health Research, but most impactfully, there were members of public who wanted to share their own stories regarding their diagnoses and subsequent treatment, and how passionately they felt about treatment options becoming available.

After this section of the meeting, the committee members went into discussion about the questions posed by the FDA in relation to the AEGEAN study. During the discussion, the consensus from the members seemed to be that whilst it was difficult to know what impact adjuvant treatment was having on the overall outcome of the outcome, the positive results from AEGEAN were difficult to ignore, and therefore should be addressed after approval. As for the voting question, the committee unanimously agreed that all future trials in this space should have a study design element that allows them to ascertain the contribution of each treatment phase, and that the FDA should be requesting this information at the study design discussion stage.

The meeting then concluded at 1.49pm US EST. Despite all of our preparation, the biometrics room were not called into action during the course of the actual ODAC meeting, although plenty of notes were taken and there were a couple of close calls when our programmers started pre-emptively working on outputs that we thought might be requested! However, this did not stop both the study team at the FDA, as well as our biometrics team from celebrating a successful meeting afterwards. Some pictures from the actual meeting have been shown in Figure 5 below.

HOW TO SURVIVE AND THRIVE WHEN WORKING ON AN ODAC

After completing work on the ODAC, I started to reflect on what went well for us as a team, the challenges we had to overcome, as well as what would make teams thrive if they found themselves in the same situation that our programming team did at the point – a bit lost, and not quite sure where to begin! Therefore, I plan on using the last part of this paper to share some of the challenges we experienced along the way, the techniques we learnt or adapted in order to overcome these and lead to a successful outcome, as well as some of the tips that I feel would allow teams to thrive in this pressured environment from the very beginning.

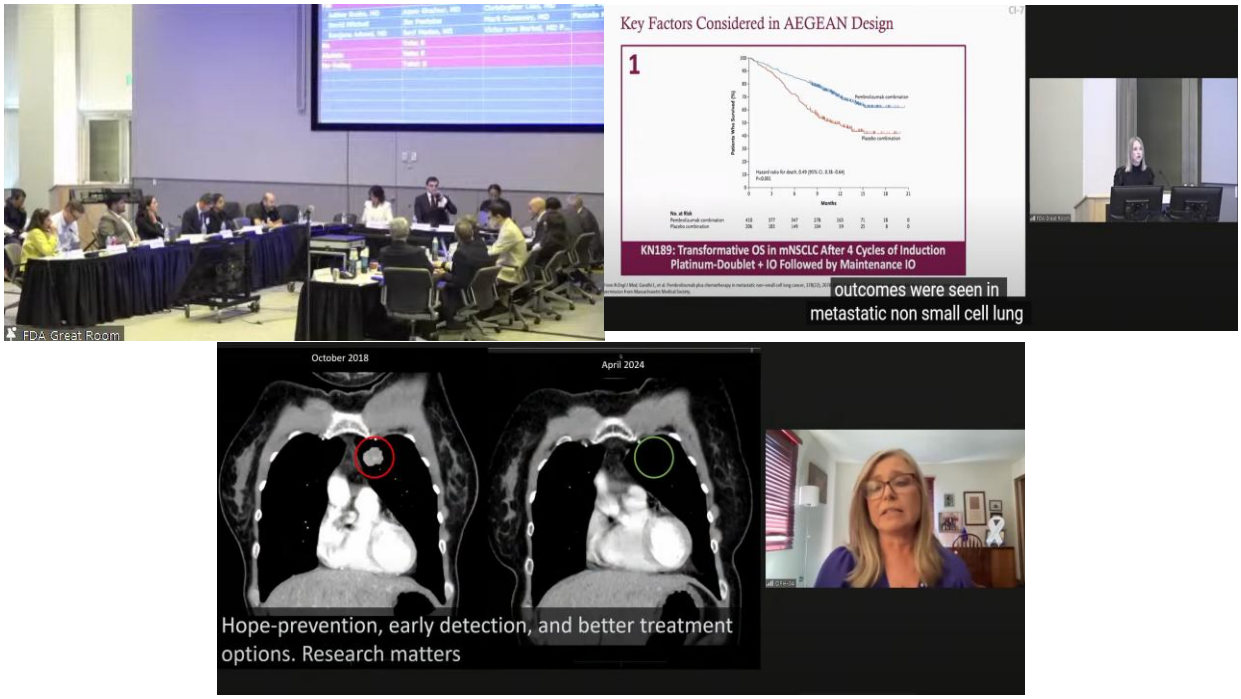

Figure 5: Images from the live stream of the ODAC. Clockwise from top left; A picture of the ODAC members sitting during the voting phase of the meeting; Leora Horn presenting a slide from the AstraZeneca core presentation; A member of the public sharing their cancer story as part of the Open Public Hearing section of the meeting.

CHALLENGES

We encountered many challenges throughout the course of the ODAC period – these can be broken down into 3 general categories to help demonstrate the challenges in general:

- **Demanding workload**: It is obvious that the additional work of preparing for the ODAC put a lot of stress and additional work onto both me and the programmers in my team. There were well over 100 additional questions that came out of the initial brainstorm across various categories, most of which related to topics that did not form part of our initial submission package. This meant having to work through specifications for how to go about producing what was being asked for and then identifying and assigning programmers who would be able to produce these quickly and to high quality. When you look at the final tally of 865 additional outputs, with an average of 3 hours to work on each side of each output, this equated to needing an additional 11 FTEs, on top of the already large amount of work that went with the existing study readouts, which also needed to be of high quality. We were nowhere near able to get the required amount of additional resource, so it meant either having to be more efficient, or working longer hours – in reality, the team and I did both. This introduced a large amount of pressure into the situation and tested both my leadership as well as the resilience of the whole team.

- **Stakeholder management**: Usually, as a Programming function we are provided the mock shells by our stats colleagues and able to get on with programming what is needed for CSRs and submissions. The ODAC was a completely different proposition, in that outputs were being discussed almost off the cuff with other stakeholders, such as Patient Safety, Clinical, Translational Medicine and PRO counterparts. These stakeholders required Programming to explain what could and couldn't be done, receiving pushback if the message was not positive, as well as then having to try and create outputs that met the needs of these stakeholders without any kind of template. We also had to manage the competing priorities and personalities that came with these stakeholders – as there were multiple demands on our function, we had to prioritize certain outputs, which then did not go down well with the function who was adversely impacted by the decision. The whole ad hoc output process was ultimately a crash course in stakeholder management, and a juggling act for a programming lead to manage and keep everything on track.

- **External pressures**: Given that the ODAC was brought in as a relatively last-minute item by the FDA, there was a lot of discussion around what the FDA might bring as part of their presentation, and this was further heightened when the FDA sent over their briefing document, which highlighted the points they intended to raise. Once this was received, there were a number of changes in the overall strategy that we were attempting to follow for certain areas of the presentation and meant changing some of the ad hoc outputs that were already scheduled to produce. Combined with this, there were some ad hoc outputs that we then realized did not answer the questions that we wanted to respond to the FDA on and therefore had to rework some of the already existing programs. As a result, it was a constant challenge to ensure that the team were working on the correct items, and to avoid needing to rework entire outputs later down the journey.

HOW WE SURVIVED THROUGH THE ODAC PERIOD

Despite the challenges that we went through, we were able to find ways of getting through these to achieve the outcome and the work we were expecting to. Again, our methods of survival can be split into 3 main categories:

- **Team morale:** It was important with the amount of work and additional pressure that we had to contend with, that I was checking in regularly with the programming team to see how they were feeling, from a morale and wellbeing perspective as opposed to a status update – the ODAC journey was a long-term piece of work, so it was important that programmers were happy with what they were being asked to do. I scheduled daily check-ins to check on their mood as well as their progress – topics were as lighthearted as what they did for the weekend, or what they had for dinner the previous evening, just to ensure everything was still OK.
  Another technique I used was to share and celebrate the small wins – when looking at the ODAC journey in its entirety, I felt that this could feel quite overwhelming, with the team always looking to the next deliverable in a pressurized environment. Therefore, I felt it was important to celebrate small wins from team members, whether that be the completion of a tricky ad hoc piece of work that was critical to a key slide in the presentation, right through to successfully managing and explaining an interaction to a cross-functional team member. Each of these mini successes contributed to the wider picture, and by celebrating them, it made the rest of the team realize that they were also contributing to the success of the wider team.
  Finally, we usually find that Programming are directed to what should be done for various outputs or pieces of work – however, given the ad hoc nature of the ODAC and what was being asked for, our function felt like an equal partner, and that was demonstrated by other functions asking for our opinions and attendance in wider team meetings, which helped boost the morale of programmers, who felt that their opinions were helping to shape the direction of the ODAC material development.

- **Understanding what was needed**: As a result of the large team involved in the ODAC, it was important to clearly define roles and responsibilities for each of the team members that were contributing. I cover earlier in the paper how we were able to redefine the GPP, SLP and back-up roles to better suit what was required of our team during the ODAC journey, but what also helped our team was to go deeper into the study team and define individual roles – whether that be letting team members know they were production or QC for the ODAC period, or letting them have a choice of which domains they wanted to work on, team members then owned the role that they were given, which led to more accountability for what was being produced.
  Following on from this, having specific Programming points of contact for other functions meant that we were able to have conversations firsthand about what was required, and work out specific considerations with the people who were making decisions – again, in usual clinical trial work, Programming are in the room but are usually the end user of any decisions, whereas for this ODAC, we were principal players in helping shape what could be done, which we felt was a success and made our work more efficient and effective.
  Lastly, I found influencing techniques to be a real strength in this environment – specifically, being able to test understanding of various concepts before committing to start programming. A lot of the discussions went off on various tangents before coming to an agreed decision about what was needed – by continuing to ask questions and check understanding of what was being said, we were able to refine the thoughts of other stakeholders in order to produce workable programming logic to meet the needs of the ODAC.

- **Communication:** Although this runs through everything we do, we found communication to be a strong characteristic in our successful interactions through the course of the ODAC. We scheduled regular check-ins with both statistical and programming staff, where the senior members of the team could share high-level messaging of what was happening for the overall ODAC, as well as giving individual members a chance to communicate any issues or concerns that they were seeing.
  As mentioned earlier, Programming played a real role in strategy meetings due to our ability to know what had already been produced, and what was possible with the data we had. Due to our willingness to share this, we found ourselves in the situation where multiple programming team members were invited to strategy meetings, in order to share our perspectives.
  As well as this, we were able to implement a speak-up culture within the function that allowed any programmer to speak up on a particular topic. This was very important, especially as the main leads for the study were so busy managing and juggling tasks, so we needed to rely on support programmers raising issues to us that we might have missed. This then translated into our interactions with other stakeholders – I certainly felt empowered to speak on behalf of Programming to challenge the position of other senior stakeholders, to ensure that all voices had been heard before we made decisions on things like which outputs might be required for a particular slide or section of the presentation.

HOW YOU CAN THRIVE THROUGH AN ODAC

Despite our survival techniques getting us through to the successful end of the ODAC, many of these were learnt or taken on board reactively, instead of proactively putting into place at the beginning of the study. Therefore, this last section of tips focusses on what can be done at the point of finding out you are going into an ODAC, that would make the project a more enjoyable (and hopefully less stressful) experience:

- **Recognizing the ODAC is challenging and novel:** Part of the initial teething issues we had on the ODAC was that we thought we would just be able to find additional resources to help support the ad hoc pieces of work that we needed to produce. In reality, this is an extremely large piece of work, that in ideal circumstances deserves its own project team just to work on it. Assuming that as a lead, you and your team would not have that luxury, I think it is important to acknowledge to your team that it is a stressful time, with a lot of programming to do, and that you are acknowledging their effort and productiveness – recognizing this will go a long way to keeping your team onside during those difficult moments.
  As it relates to ODAC-specific activities, one example of a novel piece of work is the mock meetings. We convened a smaller biometrics team for the 2nd mock meeting and gained a huge amount from the experience. However, we also had some areas where we could have been better – these ranged from not having one person speaking on behalf of each room, using Microsoft Teams with everyone from both rooms in to communicate (which led to many opinions that were probably not helpful in the moment), and everyone getting very excited and starting to talk in the room where we were watching the feed, which meant that we all missed the next (planted) question from the mock meeting. All of these things would have been avoidable had we held a preparatory meeting to discuss ways of working – this is something that wouldn't usually come up in study work, but is an example of how recognizing you are in a novel space and making plans to accommodate these new things will lead you to a more successful outcome.

- **Be adaptive:** Part of the ODAC experience for me was not knowing what was going to come up on a particular day – the conversations moved so rapidly depending on latest communications from FDA, our external advisors or internal team members, that you could be working on new outputs and domains daily. Therefore, part of thriving in this environment would be to have an agile mindset and be prepared to "go with the flow" when it comes to what you will be working on, whilst being prepared to move onto topics that were not on your radar hours previously. On the other side of this particular topic, it is also important not to take any rejection of ad hoc work personally – we found it quite frustrating on several occasions where the team had put a lot of effort into producing some outputs, only to find that it either did not answer the question the team wanted, or that things had moved in a different direction and therefore the outputs were no longer warranted. In this scenario, being able to adapt to the direction of travel of the slide deck, and embrace the change of what might be expected, will go a long way to improving your experience with the ad hoc work.

- **Teamwork**: The final area in which I feel teams can thrive is in the space of teamwork. Looking closer to home first, you will be working with a large number of programmers, all of whom will have different strengths that they could bring to the table. Where possible, try to identify those strengths early and play to them – on our ODAC, we went through a period of needing figures to be produced across a number of domains, and by asking about peoples strengths and wants, we were able to assign 2 people to just work through figures, as this was a passion and interest of theirs that they weren't able to fully utilize in their usual study work. This is also applicable for softer skills, including who you may want to have in an outward-facing role with other stakeholders.
  In terms of stakeholders, making a good first impression with other functional representatives is critical to the ongoing success of the ODAC journey – actively listening to what they want to achieve with their particular objective or slide deck, and making suggestions was a good way for our team to be quickly respected by cross-functional representatives, and made difficult conversation around priorities later in the journey much easier to handle.
  Finally, ensure you are showing an active interest in the wider team who are working on the ODAC – this can present by asking questions on certain items to test understanding or bring a different opinion to the conversation, and also to provide feedback to speakers or other presenters. This can feel daunting at the time, but we were able to do this to the lead presenter during one of the mock meetings, where we asked her to try a different wording in her responses when she wanted to make clear that the team behind the scenes and the biometrics team were to commence work. Providing the feedback in this way meant that we had a more defined gameplan for the actual meeting, should we have needed it.

CONCLUSION

Overall, I hope that this paper has set out the experiences and tasks at hand that go into preparing and delivering when called up to an FDA ODAC meeting. I found the experience to be both extremely challenging in terms of my programming project management, stakeholder relations, and general ability to keep track of multiple data cuts and deliverables, but also extremely rewarding when you see how many functions and representatives who don't usually work closely, came together as a group to get through an extraordinary amount of work and development, in order to argue the case for a new regimen to treat lung cancer patients. The best way of explaining the impact of the work we did was when the primary goal from the meeting was realized 3 weeks later, as the FDA went on to approve the AEGEAN regimen in the United States. I am both proud of the impact that I made to this key milestone, and grateful for the chance to experience an ODAC, as I consider this one of the highlights of my career – whilst never forgetting the achievements and stress that went with it! Hopefully, this paper will guide you in the right direction should you ever find yourself preparing for an ODAC, so you can enjoy both a similar outcome and sense of achievement.

REFERENCES

1. Oncologic Drugs Advisory Committee | FDA: https://www.fda.gov/advisory-committees/human-drug-advisory-committees/oncologic-drugs-advisory-committee
2. July 25, 2024 Meeting of the Oncologic Drugs Advisory Committee Meeting Announcement: https://www.fda.gov/advisory-committees/updated-agenda-information-july-25-2024-meeting-oncologic-drugs-advisory-committee-meeting

ACKNOWLEDGMENTS

I would like to acknowledge Jinesh Patel, Charles Wright, Ruth Doake and Helen Mann from AstraZeneca, who were critical to the ODAC process as fellow statistical and programming leads and oversights, and who supported me in developing the content for this paper. A special thanks also goes to the programmers who worked in my team on the various deliverables during this period; there are too many to name check all, but without whom this experience would not have been as successful and rewarding as it ultimately ended up being.

Finally, I would like to thank my wife Beckie, who went through the ups and downs with me whilst I was going through the ODAC and has been supportive enough to relive it with me whilst I was authoring this paper.

CONTACT INFORMATION

Your comments and questions are valued and encouraged. Contact the author at:

Zach Dorman
AstraZeneca
Email: zach.dorman@astrazeneca.com
LinkedIn: LinkedIn - Zach Dorman