

How to streamline a complex process: why experienced medical writers will add value to oncology dossiers

Julia Forjanic Klapproth, senior partner, and **Maurice Löwens**, medical writing manager at Trilogy Writing & Consulting, discuss how medical writers can smooth the process of producing oncology dossiers.



Oncology is one of the most common areas of drug development in the pharmaceutical industry. In 2020, many of the new drugs approved by the FDA were cancer treatments. Existing cancer drugs are also regularly being approved for additional indications (<https://blog.navitus.com/specialty-pipeline-2021>). The submissions needed to get these approvals are the result of large numbers of oncology studies that are being run all over the world. The summary documents for these submissions are often large and complex and having experienced medical writers to work with the clinical teams, who are aware of the unique aspects of oncology studies and have an understanding of the principles underlying cancer therapies, will help pull these documents together more easily and ensure they are communicating the key messages clearly.

Cancer is a disease that is frequently treated over the long term, and even when the cancer has been eliminated, follow-up continues for years. As a result, the end points to assess efficacy tend to look at the effect over time and its endurance, not just a static assessment of whether the disease is cured, as in many other therapeutic areas. The challenges associated with this in the context of submission dossiers arise from the fact that there are often multiple interim study reports, in addition to the final CSR (clinical study report), and multiple data cuts over time (sometimes with different data cuts across multiple studies, which can be tricky to explain to the reader of a submission). Cancer therapy is also a dynamic area, with developments in biotechnology rapidly shifting the approach to treatment. The medical dogma in many cancer types can shift swiftly, which means that the scientific rationale, available treatments, and medical need descriptions must often be updated frequently – sometimes changing considerably, even within a 12-month period, as new treatment options alter the therapeutic landscape.

The role of the medical writer in the dossier-writing process is to collaborate with the clinical experts to understand their vision for the treatment being studied and to crystallise the messaging from the clinical programme. The medical writers need to come to terms with the oncology-specific terminology, acronyms and efficacy endpoints (progression-free survival, overall response rate, duration of response). They

also need to work with the clinical teams to know where current changes in the medical opinion might need to be reflected in the medical need discussion and to understand how the product under assessment needs to be positioned in the overall picture of available therapies. Frequently, because the clinical experts are often deeply involved in the research going on in their area, the medical writers need to help the experts step back from the minutiae and look at the big picture in the context of a registration dossier. It is important that the regulatory documents stay focused on what is needed to get regulatory approval of the target product profile (TPP) and not get off target and bogged down by academic questions (that can be interesting but should be saved for publications).

To do this effectively, it is essential that submission teams have a clear and well developed TPP from the start of a clinical development programme. Ideally, the programme should be reverse engineered to specifically collect the data that will be needed to support the intended claims of the TPP. At the latest, it should be ready by the time writing on a submission dossier begins. Without the TPP, it can be challenging to know what aspects to focus on in the Module 2 summaries. If written in parallel, it often gets in the way of writing the dossier as the team chases a moving target. Having the TPP ready and agreed on well in advance gives the team clarity on what issues to focus on throughout the clinical programme, in general, and when writing the CTD (common technical document) summaries, in particular.

During an oncology clinical programme, it is not uncommon to have multiple dose modifications as the investigators adapt to manage AEs and slowly home in on the optimal dose regimen. Early studies can have different dosing regimens than later studies. As a result,

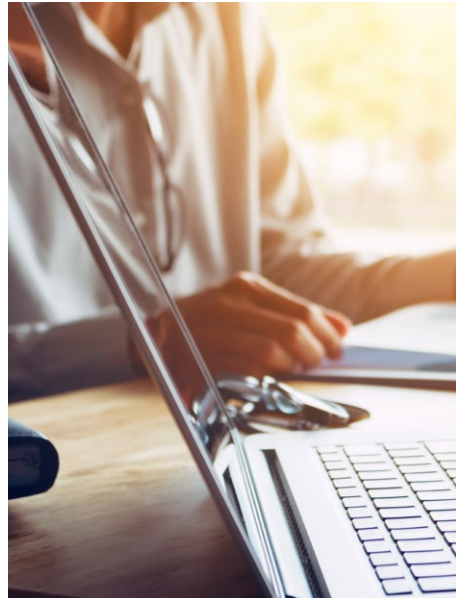
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treatment groups can be very fragmented, making it difficult to interpret the data, particularly in a pooled dataset, because the data cannot be easily compared across different doses. Changes in dosing can also mean that the proposed dose has less exposure time than earlier ones. These issues affect the interpretation of both efficacy and safety and need to be considered carefully when planning how to present the data in the dossier.

Another hurdle that teams often grapple with when writing oncology dossiers is how to handle an adverse event of special interest (AESI). Due to the different organs affected with different cancers, there is often little consistency in the AESIs collected in different studies. This presents a challenge when summarising them across studies in Module 2.7.4. Do you try to find a consistent grouping of these across studies in different cancer types, or do you just present AESIs from the pivotal trial? In oncology, the AESIs will be driven by the risk factors from the underlying disease (cancer type) and in a large dossier, you will need to find a way to bring some very diverse safety data together. This should be thought about as early as possible when the team begins to plan for the dossier, and it certainly needs to be discussed in the statistical analysis plan (SAP) for the safety summaries.

Kaplan-Meier plots are widely used in oncology programmes for the depiction of overall survival, as well as the time to onset and time to resolution of adverse events. These plots can be very useful in visualising how much of a difference there is for the duration of survival in patients treated with the drug under assessment versus other treatment options. Similarly, in the context of adverse events, Kaplan-Meier plots can help make clear the periods of risk for drug-related events. It is helpful for medical writers to understand how Kaplan-Meier plots work, so they can provide context when writing about these.

Something else to keep in mind when planning the dossiers, is whether there is a likelihood of submitting in other regions (eg Japan). If so, it is a good idea to discuss this with colleagues from those other regions, while developing the SAPs for the efficacy and safety summaries, to be sure that all analyses will be planned as required or expected by their local agencies. There is nothing more frustrating than thinking the dossier is fit-for-purpose for a global submission, only to find out that you need



additional analyses to be run and incorporated. The value of having an experienced medical writer on the team is that they will be thinking about many of these challenges in advance and can bring meaningful advice and guidance to the dossier team. While subject matter experts are focused on their particular area of expertise, a medical writer is far enough away from the minute details to be able to add value to ensure the documents stay focused and fit for purpose.

Medical writers often come to the project with a fresh pair of eyes and they can ask the simple questions that the team may have overlooked. Their experience in writing submission dossiers can streamline the planning and writing process, helping the team navigate a minefield of potential problems and letting the subject matter experts spend more time on crafting the messages. With a strong regulatory lead who has a good vision of the target, and clinical experts who understand the therapeutic benefits to be gained, a strong medical writer rounds out a dossier team by advising on how to present the information in order to direct agency reviewers to what they are looking for and aid the approval process. ●

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