How to Streamline a Complex Process: The Value Add of Experienced Medical Writers for Oncology Dossiers

Oncology is one of the most common areas of drug development in the pharmaceutical industry. In 2020, the majority of new drugs approved by the FDA were cancer treatments.[1,2] Existing cancer drugs are also regularly being approved for additional indications.[2] 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 working 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 endpoints 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, 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 very 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, currently available treatments, and medical need descriptions often need to be updated frequently – sometimes changing considerably, even within a 12-month period, as new treatment options change 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 program. 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 bogged down and off target in academic questions (that can be very interesting but should be saved for publications).

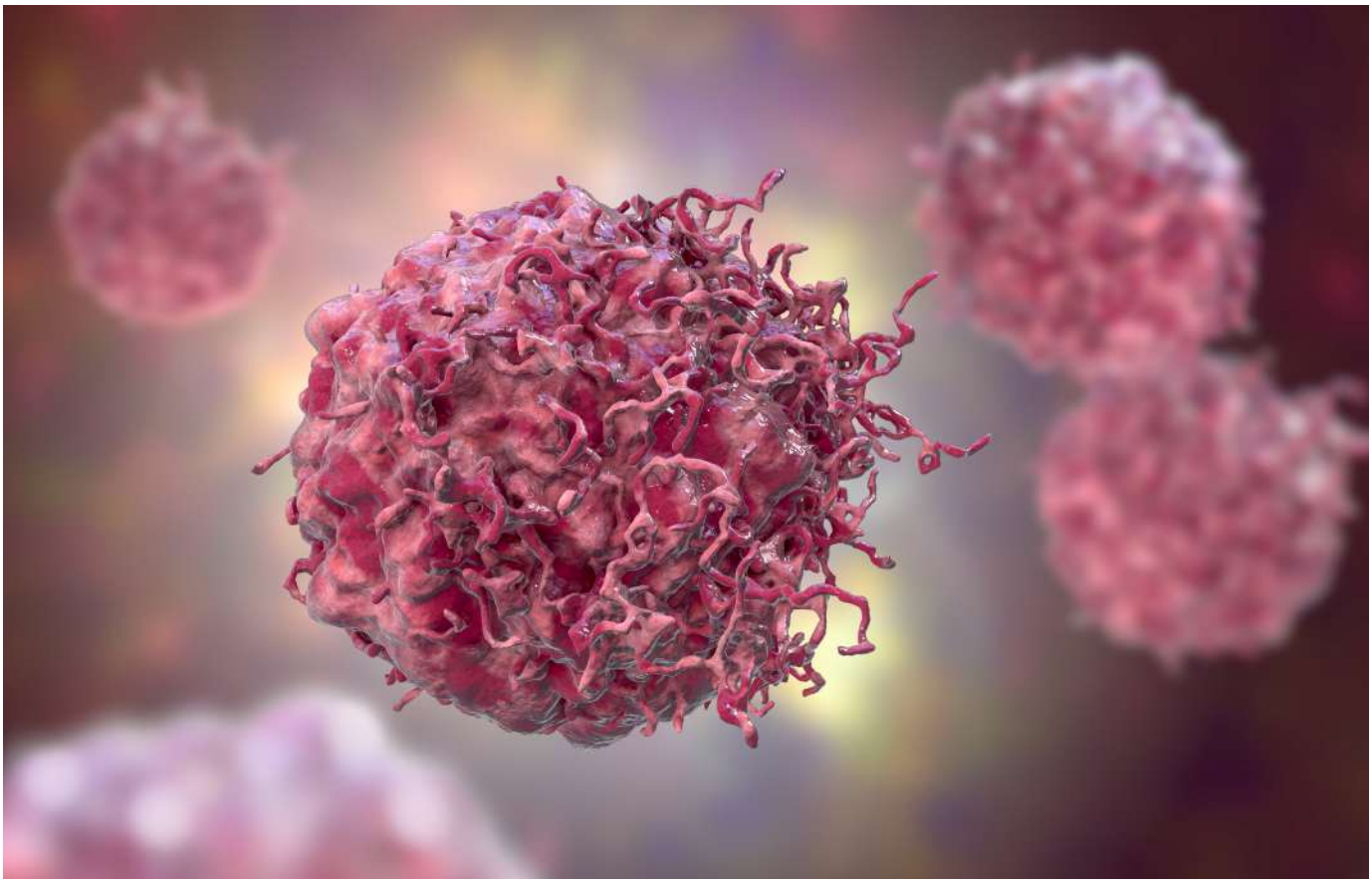
To do this effectively, it is essential that submission teams have a clear and well developed TPP from the start of a clinical development program. Ideally, the program should be reverse engineered to specifically collect the data that will be needed to support the intended claims of the TPP. At the 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 program, in general, and when writing the CTD summaries, in particular.

During an oncology clinical program, 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, treatment groups can be very fragmented, making it very 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 doses. These problems 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 adverse events of special interest (AESIs). Due to the different organs effected 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 programs 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 visualizing how much of a difference there is for the duration of survival in patients treated with the drug under assessment vs 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 useful context when writing about these.

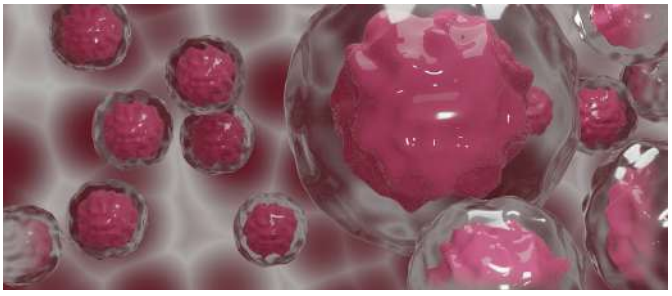
Something else to keep in mind when planning for and writing oncology dossiers, is whether there is a likelihood of submitting in other regions (e.g. Japan). If so, it is a good idea to have a discussion with the colleagues from those other regions while developing the SAPs for the efficacy and safety 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 into the files.



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 naïve questions that the team may have completely 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 with clarity that will direct agency reviewers to what they are looking for and aid the approval process.

REFERENCES

1. New Oncology Drug Approvals in 2020. Clinical Oncology News. 15 Dec 2020
2. In the Pipeline: Specialty Drugs to Watch in 2021. Accessed online at In the Pipeline: Specialty Drugs to Watch in 2021 (navitus.com)



Julia Forjanic Klapproth

After receiving her PhD in developmental neurobiology, Julia started her career as a medical writer in the regulatory group at Hoechst Marion Roussel (later Sanofi) in 1997. Since then she has been president of the European Medical Writers Association (EMWA) twice (2001–2002, 2007–2009). In 2002, Julia co-founded Trilogy Writing & Consulting, a company specialised in providing regulatory medical writing. In addition to managing the company as President/Senior Partner, she writes a wide array of clinical documents including study protocols, study reports, and is specialised in the clinical parts of CTD submission dossiers.

Email: julia@trilogywriting.com

Maurice Löwens

Maurice studied Natural Sciences at Cambridge University and spent 4 years in pharmaceutical manufacturing before discovering the world of regulatory writing. He now has over 14 years' experience as a medical writer and has been with Trilogy Writing & Consulting for 3 years. He has worked on numerous types of clinical regulatory documents and enjoys collaborating with diverse teams of experts from across drug development. In his current role as a Senior Medical Writing Manager, he leads teams of writers on a wide variety of regulatory writing projects.

Email: maurice.loewens@trilogywriting.com