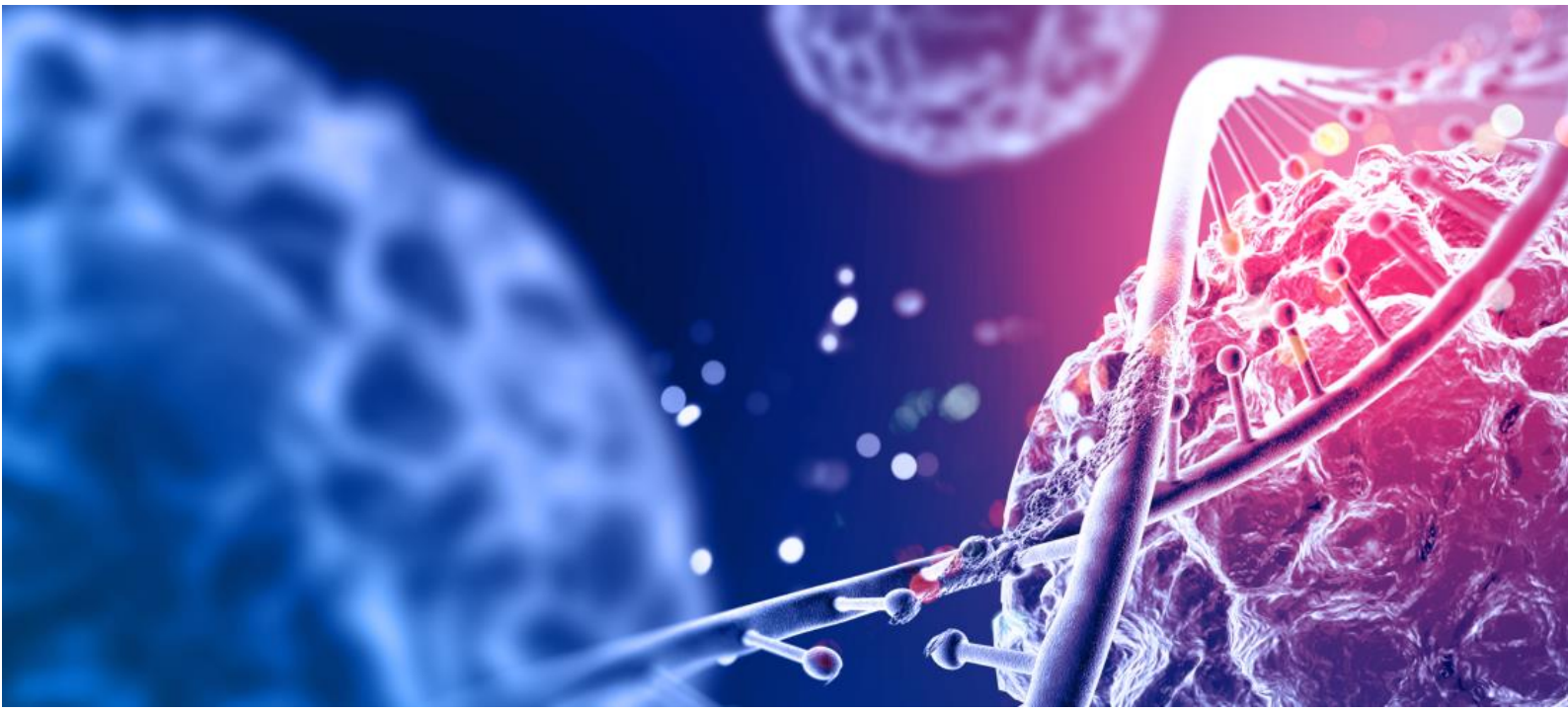
Onco trat™

ONCOLOGY FORECASTING



Essentials for Robust Oncology Forecasting & Market Valuations

The foremost thing you need to know about forecasting in the oncology area is that you will most likely be dealing with a highly dynamic therapeutic area with its own peculiarities.

Most analysts when faced with an oncology forecast can find it quite daunting since oncology is a highly specialised and technical area mixed in with plenty of seemingly impenetrable terms.

Let's break the problem down into bite sized chunks that we can digest more easily…

Black Swan Analysis™

Contents

Patients & epidemiology

Oncology is always reported and thought of in terms of ‘incidence’, that is new cases per time period (most likely a year), rather than many markets that are concerned with ‘prevalent’ patients – total number of patients with a condition at any given point in time. This is a significant variation from more traditional disease areas and needs to be accounted for when building a forecast model.

Furthermore, oncology patients are staged at point of diagnosis, regardless of how they progress. A patient diagnosed with Stage 1 lung cancer can progress, however they will never be termed as a Stage 4 patient. They may be termed to have progressed to advanced metastatic disease or have a relapse, but their staging does not change.

Special attention should be paid to calculating the eligible patient population that feeds the starting block of the forecast model, patients need to flow through a model from diagnosis to the therapeutic setting of interest.

Factors to consider:

1. Stage of patients at diagnosis
2. Staging classification that should be applied (if different from AJCC)
3. Histopathology (if relevant)
4. Age and co morbidity status
5. Other exclusion or inclusion criteria (e.g. symptoms, fitness for treatment, tumour size & position etc)

Eligible Patient Populations

This brings us neatly on to what the eligible patient population or populations for consideration are likely to be. From the clinical development plan, it should be clear (well, relatively clear) whether you are looking at patients new to treatment or those that have progressed from earlier lines of therapy. The reason for the progression may also dictate which eligible populations you should be considering.

Mutations & Biomarkers

Broadly within the remit of epidemiology, is the issue of biomarkers and mutations. Many new biological therapies currently in development, are geared toward a specific subset of patients, with a specific biomarker or mutation. This is more common in oncology than in any other therapy area.

Remember that for some cancers, biomarkers / mutations are in their infancy and thus may be future disruptors that are likely to shape the oncology market. These should be included where possible in order to future proof your model.

Factors to consider:

1. Research into identification of novel biomarkers or mutations that significantly predict differential outcome from treatment (e.g. patients with mutation fare significantly worse or better than the overall population with this type of cancer)
2. Products being developed for patients with specific mutations or biomarkers – these could force a fragmentation of the market
3. Driver mutations that only occur after treatment with a specific product or class of products
4. Subsequent exclusion or inclusion criteria based on prior treatment

Relapse vs. Refractory vs. Line of Therapy

In amongst the eligible patient population segments, there are likely to be those patients that have f failed on a treatment or failed in a treatment setting. Are the patients you want to include those that relapsed (i.e. failed on a therapy that they had previously responded to) or possibly those that are c 'refractory' (i.e. not responded to their current therapy within a specified time period)? Do you need different lines of therapy within your model or previous treatment settings?

Target patient settings to consider:

1. Treatment naïve
2. Relapse or refractory
3. Patients failing on treatment with "x"
4. Adjuvant or neoadjuvant treatment
5. Maintenance therapy

Therapeutic focus / selection

Treatment of oncology patients can be multi-modal in that patients can undergo surgery (often referred to as resection), radiotherapy, chemotherapy, various targeted or locally delivered therapies, as well as immunotherapeutic options. These are not necessarily mutually exclusive, but you need to determine what is critical to include within your forecast model. Take care to include anything that has potential to disrupt the market or significantly affect the number of eligible patients you are considering; an example of this being treatments that are earlier in the patient management process that could be curative, reducing patients through the treatment flow.

Each cancer has its own set of treatment options from radioactive iodine treatment in some types of thyroid cancer to TACE (Transarterial Chemoembolization) in hepatocellular carcinoma.

Essential dynamics to include

We have spent some time considering the patient population and treatment landscape, (all essentials to be included within any good forecast) but let's now think about other dynamics and market drivers that should be included within an oncology forecast.

Some forecasts may include compliance, however as here as adherence to cancer medications is typically very high, this is not usually required in an oncology forecast. However, persistence or rather treatment duration, is of paramount importance; in an incidence-based model it has a substantial impact on revenue calculations.

Not only does treatment duration drive product use, it can also be a disruptive event. Consider the following situation: my product is due to launch in the treatment of patients in the relapse/refractory setting in our specific market, but a novel therapeutic product is

launching in first line treatment in the same market. This novel therapeutic extends the average duration of treatment in the first line setting from 6 months to 24 months. This has a direct impact on the rate of flow of patients coming off first line and moving to a second line treatment option (part of our eligible market). The extent to which this is a problem will depend on the share of patients that this novel therapeutic gains in the first line setting – if they only gain 2% share, it's unlikely to have a material impact, but if they gain 60% share, then our second line pool will be impacted.

Disruptive Events – Points of Market Evolution

As well as those items already mentioned above (mutations, biomarkers etc), there are many places that disruption can come from within the oncology sphere. Here are examples of a few:

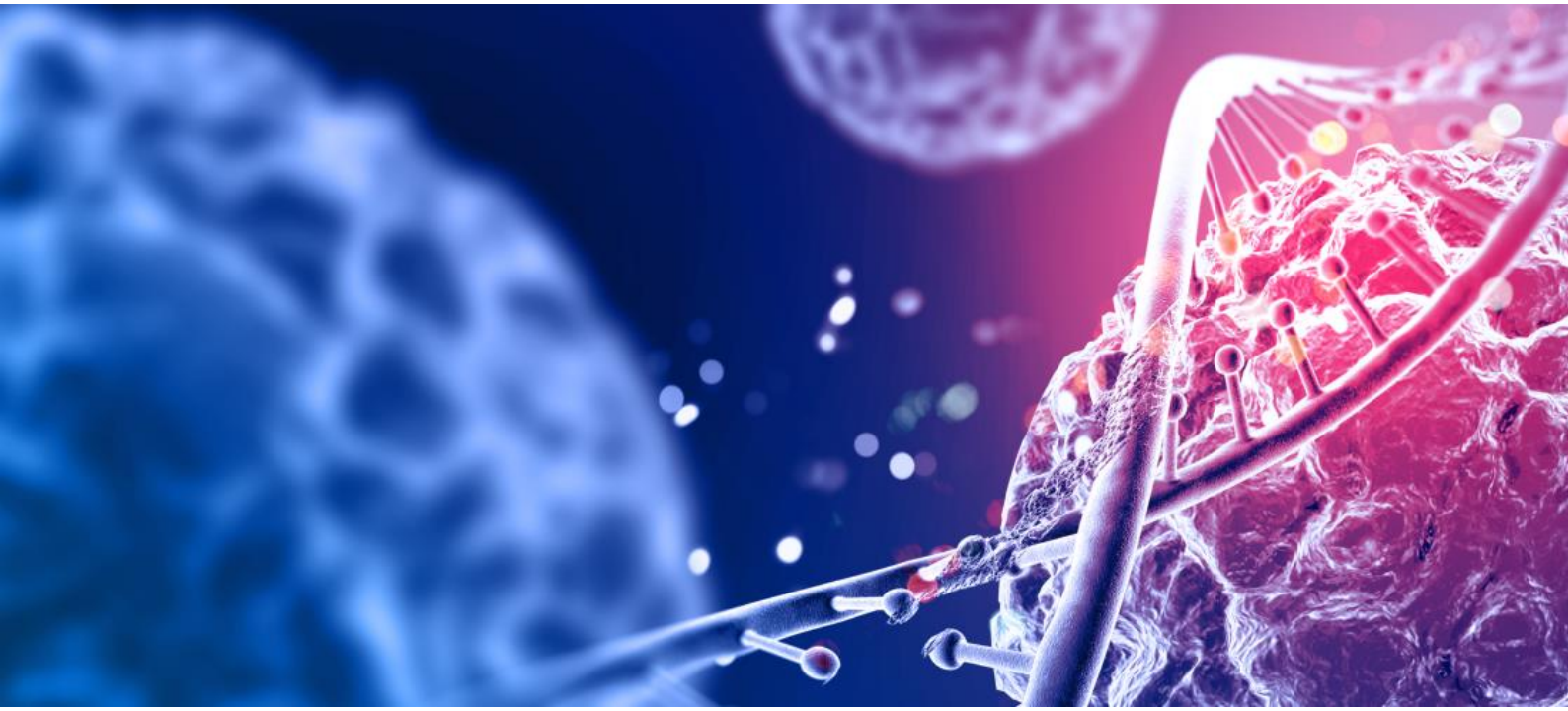
1. Impact of vaccines and successful treatments on cancers caused by infectious agents – these are quite insidious since they often take many years to impact the market but can destroy a viable market completely. Examples include HCV treatment, HPV vaccination.
2. Removal of an identified risk factor for a cancer (similar to point 1) – a prime example of this is smoking and lung cancer, but there are many others.
3. Cancer vaccines – rather than removing a causal agent, these 'cure' the cancer itself. It is arguable whether some of the agents that could fall under this category are true "vaccines" but think about those treatments such as T-VEC that have

astounding results on reducing inoperable malignant melanomas. There are many of these types of technologies in development and while they may be thought of as ‘outliers’, these are exactly the type of disruptors that should be considered carefully when building the forecast model.

4. Upstream market events – while in the classical sense when forecasting it is tempting to only include those products that are scheduled to launch with a similar indication to our product and thus compete directly for patient share, within oncology we cannot afford so narrow a focus. Oncology **product** forecasts really should be oncology **market** forecasts since a disruptive product can launch anywhere along the patient flow but will disrupt anything downstream of it.

Dynamic patient flow

For all the reasons listed so far, the only way to accurately forecast an oncology product is with a dynamic patient flow model, where patients in downstream lines of treatment have been directly fed from upstream patient pools. By controlling the flow rate between these pools or lines of therapy, it is possible to model the market and produce a robust, transparent oncology model capable of accurately depicting even the most complicated of oncology environments. Because oncology is driven by incidence epidemiology data, and is also commonly treated disease progression, we are left with dynamic patient flow as most efficient method of fully capturing the unique features of a complex, evolving marketplace.



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