



PACIFIC LIFE RE

The evolution of targeted cancer therapies

This article is our second which looks at findings presented at the American Society of Clinical Oncology's annual conference in Chicago in June. In our first article we looked at potential forthcoming improvements in cancer diagnostics, focusing on tests which aim to detect cancer at earlier stages. Here we look at refinements in the use of targeted cancer therapies. Once almost exclusively used for advanced disease, recent scientific work shows their use could be expanded to patients with other stages of disease.



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Targeted therapies for earlier-stage disease

More and more cancer research is being undertaken which specifically investigates targeted therapies. Drugs which are tailored to specific sub-types of cancer and/or the genetic make-up of patients increasingly supplement or replace the 'blunt tools' of chemotherapy and radiotherapy which have long been the mainstays of treatment for many cancers. The usage of targeted therapies has tended to focus on patients with late-stage disease for whom other treatments have failed or have stopped working. This is for a number of reasons including their side-effect profiles and the expense associated with their use. However, two developments announced in Chicago hint that this may be changing and usage of these drugs in earlier stage disease may be about to accelerate.

Mid-stage breast cancer

The first of these relates to the drug **ribociclib** and to its usage to treat some **breast cancers**.¹ A recent trial found that when this drug is added to hormonal therapy, after surgery to completely remove a tumour, the number of recurrences in the next three years fell by 25%.

This is exciting because it relates not only to a common type of cancer (breast) but to a common sub-type, known as 'HR-positive, HER2-negative' which accounts for around 70% of all cases. Patients in the trial had early- and mid-stage cancers, defined as stage 2 and stage 3. 9.6% of patients who received three years of treatment relapsed during the study period, whereas this occurred for 12.9% of those who did not receive the drug. These results were achieved despite scientists administering a relatively low dose of the drug

which helped to reduce side-effects to tolerable levels, most often including joint pain and hot flashes.

Data up to 2018 suggests typically 90% of women with stage 2 cancer will survive for at least five years, while only 70% will survive this long if their cancer is diagnosed at stage 3. Breast cancer accounts for around 42,000 deaths each year in the USA², and around 11,500 per year in the UK.³

Typically, around one-third of breast cancers are diagnosed at stages covered by this trial, and are of the relevant type. We only have data for a few years, and don't know the long-term impact of this drug on survival. It is also the case that because survival at these earlier stages is much better than at Stage 4, more patients need to be offered this



treatment to materially improve outcomes. However, it's clear that even the potential to delay progression for women eligible for ribociclib could have significant impacts on mortality.

Lung cancer drug



A second success announced related to the drug **osimertinib** and its usage to treat some **lung cancers**.⁴ Lung cancer is the leading cause of cancer deaths worldwide. This time, the drug was used on people with the most common subtype of lung cancer (non-small cell lung cancer; NSCLC) and who have a mutation known as EGFR. It was used on people with stage 1B, 2 and 3A cancers – essentially covering most early- and mid-stages.

The EGFR mutation is present in 10-25% of people with lung cancer in North America and Europe, but more like 30-40% in Asia.⁵ EGFR mutations can cause cancer cells to divide and grow, and osimertinib blocks this action.

Headline results

The headline results were that while only 78% of people who took a placebo were still alive after five years, this rose to 88% among those who used osimertinib. In other words, deaths approximately halved in the group using this drug. Interestingly, two-thirds of participants had no history of smoking (non-smokers who get lung cancer disproportionately tend to have the EGFR mutation). It will be interesting to see when the full results are published, whether the headline figures hold true in a cohort which more accurately reflects global lung cancer sufferers, who skew heavily towards smokers, including current smokers.

The drug is also being evaluated in other stages of lung cancer, including when it is used before patients have surgery.

Both ribociclib and osimertinib have the potential to significantly improve patient outcomes in quite substantial groups of patients. This in itself is exciting and the changing usage of targeted therapies is further cause for hope. While these are not the very first targeted therapies to be used to treat early stage cancers, they may be a sign of a flood of further therapies to come in the coming years.

Conclusion

It is easy to take for granted the year-on-year improvements in cancer survival we have seen continuously for many years. When we talk in abstract terms about survival it is easy to lose sight of the work that goes into achieving this. The above developments are each likely to incrementally improve survival for a material but small proportion of all cancer sufferers. Getting each of these drugs to the point where they may be approved for use involves years of scientific research and often significant sacrifices from trial participants.

Cancer is composed of so many types and sub-types of disease that individual new drugs or techniques are likely to do no more than chip away at the edifice of cancer mortality. However, while none of these may currently constitute a 'game changer' for cancer survival overall, each of them is likely to make an enormous difference for significant numbers of patients for whom these techniques or drugs are the difference between good health and poor health, or between life and death.



References

- 1 [NATALEE: Ribociclib With Hormonal Therapy Cuts Recurrence Risk by 25% in Most Common Type of Breast Cancer \(ajmc.com\)](#)
- 2 [Basic Information About Breast Cancer | CDC](#)
- 3 [Breast cancer statistics | Cancer Research UK](#)
- 4 [Program Guide – ASCO Meeting Program Guide](#)

Around 85% of people with lung cancer have NSCLS, so the proportion eligible for this therapy might not be far below these figures, in theory. However, Stage 4 is the most common stage at diagnosis, and to achieve the benefits seen in this trial the cancer should be no further progressed than Stage 3A, and the earlier the better.



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