

How to start and end the Discussion

This pdf shows four openings and closings of different discussion sections. The opening parts display different ways to open your discussion: by a short recap of the study's aim or hypothesis, the contribution of the paper —or a combination of those, but they all end up with presenting the major finding(s). You can also skip all the run-up and start out with stating the major findings. The closing parts relate to the opening paragraphs by addressing the hypothesis or aim again, pointing at implications (related to the contributions), and future research connected to this study.

1. Contribution, aim, focus, findings

This is the largest study evaluating the presence, including the composition, of ductal carcinoma in situ-associated immune cells in relation to ductal carcinoma in situ subtype based on immunohistochemistry. In our series, we found an association between ductal carcinoma in situ subtype and the presence of TILs, whereby ER-PR-HER2+ and triple-negative cases had the highest numbers of TILs, which is in line with previous studies.

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In conclusion, high numbers of TILs are mainly observed in HER+ and triple-negative ductal carcinoma in situ and the majority of these are CD4+ T cells. The ER+HER2+subtype seems to attract a higher proportion of CD8+T cells compared with the triple-negative subgroup. In addition, the TIL-high HER2+ subgroup (independent ofER) had the lowest PD-L1-SP142 expression on tumor cells. This suggests a more pronounced antitumorigenic immune response in HER2-positive ductal carcinomain situ, which might play a role in its distinct biological behavior.

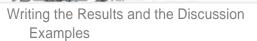
2. Focus, hypothesis, findings

This single-center prospective study assessed the real-world clinical utility of plasma-based genotyping in patients with metastatic NSCLC. We hypothesized that adding plasma NGS would increase detection of therapeutically targetable mutations and allow personalized therapy for more patients. Therapeutically targetable mutations were detected in 113 of 323 patients (35.0%) overall. Importantly, mutations for 35 of 113 patients (31.0%) were detected in plasma only when tissue DNA was insufficient or unavailable, or no mutation was detected in tissue. Targetable mutations were detected for 31 patients in plasma and tissue. In 16 patients, targetable mutations were found in tissue only.

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Conclusions

This clinical study is, to our knowledge, one of the largest to measure the implications of plasmabased genotyping for the delivery of targeted therapy in NSCLC and clearly demonstrates that liquid biopsy can improve delivery of therapy and, consequently, outcomes. To keep up with rapid therapeutic progress in the molecular diagnosis and treatment of NSCLC, we must incorporate safe and facile non-invasive methods for sensitive, comprehensive tumor profiling to select patients for



personalized therapy. Given the ease of obtaining plasma-based genotyping and the success observed with such a non-invasive approach, our results argue for incorporation of plasma-based genotyping into routine clinical management of patients with NSCLC.

3. Aim and contribution, findings

Our results seek to provide clarity and refine the estimate of the cost to develop a single oncologic drug. Specifically, we found that the cost to develop one cancer drug is approximately \$648.0 million (\$757.4 million when opportunity costs are included), a figure that falls between prior estimates but is significantly smaller than a widely publicized figure of \$2.7 billion.

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Conclusions

Prior estimates for the cost to develop one new drug span from \$320.0 million to \$2.7 billion. We analyzed R&D spending for pharmaceutical companies that successfully pursued their first drug approval and estimate that it costs \$648.0 million to bring a drug to market. In a short period, development cost is more than recouped, and some companies boast more than a 10-fold higher revenue than R&D spending—a sum not seen in other sectors of the economy. Future work regarding the cost of cancer drugs may be facilitated by more, not less, transparency in the biopharmaceutical industry.

4. Contribution, aim, findings

To our knowledge, this study is the first to reliably examine the risk of BC after HL according to radiation volume. Mantle field irradiation was associated with a 2.7-fold increased risk of BC compared with mediastinal irradiation alone. Our results support the hypothesis that reducing the proportion of breast tissue exposed to radiation will indeed decrease the future risk for BC, the most important late treatment effect among female survivors of HL.

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In summary, women treated with RT for HL before the age of 41 experience a high risk for BC. Our results show that reduction of radiation volume can lower this risk. Gonadotoxic treatment can also reduce the future risk for BC, especially when menopause occurs relatively shortly after treatment. The beneficial effect of gonadotoxic treatment is present in women treated before age 31. Women treated between age 31 and 40 do experience an increased risk for BC, but this risk is not reduced by gonadotoxic treatment, possibly because there are fewer years before natural menopause occurs in these patients. When confirmed by others, these findings may have implications for BC screening in female HL survivors.

Sources:

- 1. https://doi.org/10.1038/s41379-019-0331-8
- 2. doi:10.1001/jamaoncol.2018.4305
- 3. DOI:10.1001/jamainternmed.2017.3601
- 4. DOI: 10.1200/JCO.2008.19.9174