



ASO Author Reflections: What Role Do Surgeons Play in the Era of Effective Systemic Therapy for Melanoma?

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PAST

Before the introduction of effective systemic therapy, metastasectomy was considered an important therapeutic option for carefully selected patients with stage 4 melanoma. Whereas historically, systemic options were associated with low response rates and median survivals measured in months, complete resection could achieve 5-year overall survival rates of up to 40%.¹ Development of immune checkpoint inhibitors and molecularly targeted agents has altered the therapeutic landscape, necessitating reexamination of the role played by metastasectomy in stage 4 melanoma.² How has the availability of these drugs changed selection for surgery? Does metastasectomy still appear to contribute to improved outcomes? Should it come before systemic therapy or afterward?

PRESENT

Nearly half of the 2353 eligible patients in this study underwent surgical treatment, and the familiar advantage in this group overall was observed. The findings also showed the striking impact of modern drugs, with a more than 70% reduction in the risk of melanoma death with the use of

modern agents. Did this affect selection for surgery? It did not appear to make selection stricter because the proportion of surgical patients actually increased, and fewer selection factors were significant in the modern era. Does resection of stage 4 disease offer a survival benefit when modern drugs are used as well? It would take a randomized trial to be sure, but the results of this study suggest that this is indeed possible. Both multivariable analyses and matched-pair examinations showed that resection was associated with significantly better survival. Selection bias remains a concern, as it has always been in this type of study, but a therapeutic effect of metastasectomy still appears to be a reasonable possibility.

FUTURE

Is it possible that surgery makes modern drugs work better? Recent trial data demonstrate that the efficacy of modern systemic therapies may be greatest among patients with low-volume disease,^{3,4} and they may work best in the adjuvant setting when no disease is clinically apparent.^{5,6} These data add to the rationale for considering metastasectomy in the present. Outside the context of a clinical trial, this must be done with input from multiple disciplines and with careful estimation of risks and benefits. But surgery must not be forgotten as an option, particularly given the findings of this study. More study in the form of prospective trials is clearly needed to define the best way to care for patients with metastatic disease. Should surgery be used up front to cytoreduce? Should a period of initial medical therapy be used to avoid futile operations? Clinicians owe their patients and those of the future their best efforts to answer these questions.

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ASO Author Reflections offer a brief invited commentary on the article, Impact of Effective Systemic Therapy on Metastasectomy in Stage IV Melanoma: A Matched-Pair Analysis. *Ann Surg Oncol*. 2019. <https://doi.org/10.1245/s10434-019-07487-5>.

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