



Penn Medicine

18<sup>th</sup> Annual Focus on Melanoma

# Who Needs Adjuvant or Neoadjuvant Therapy?

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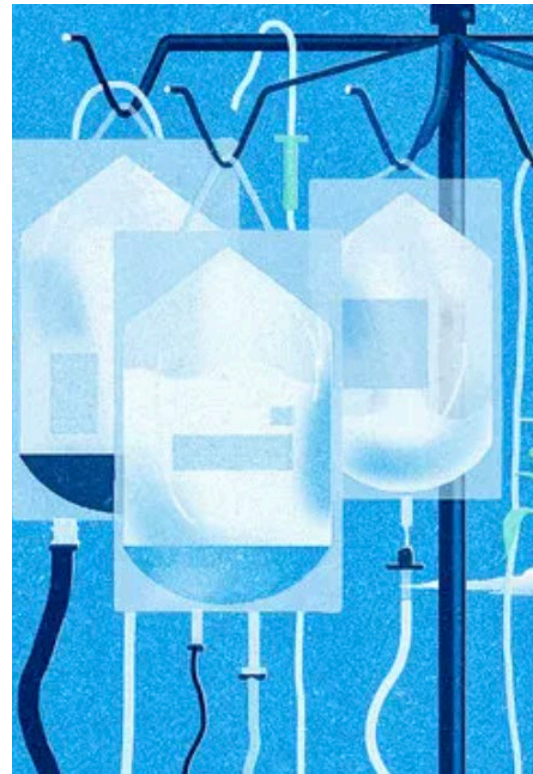
Friday, May 21, 2021



# What is adjuvant therapy?



Surgery



Treatment



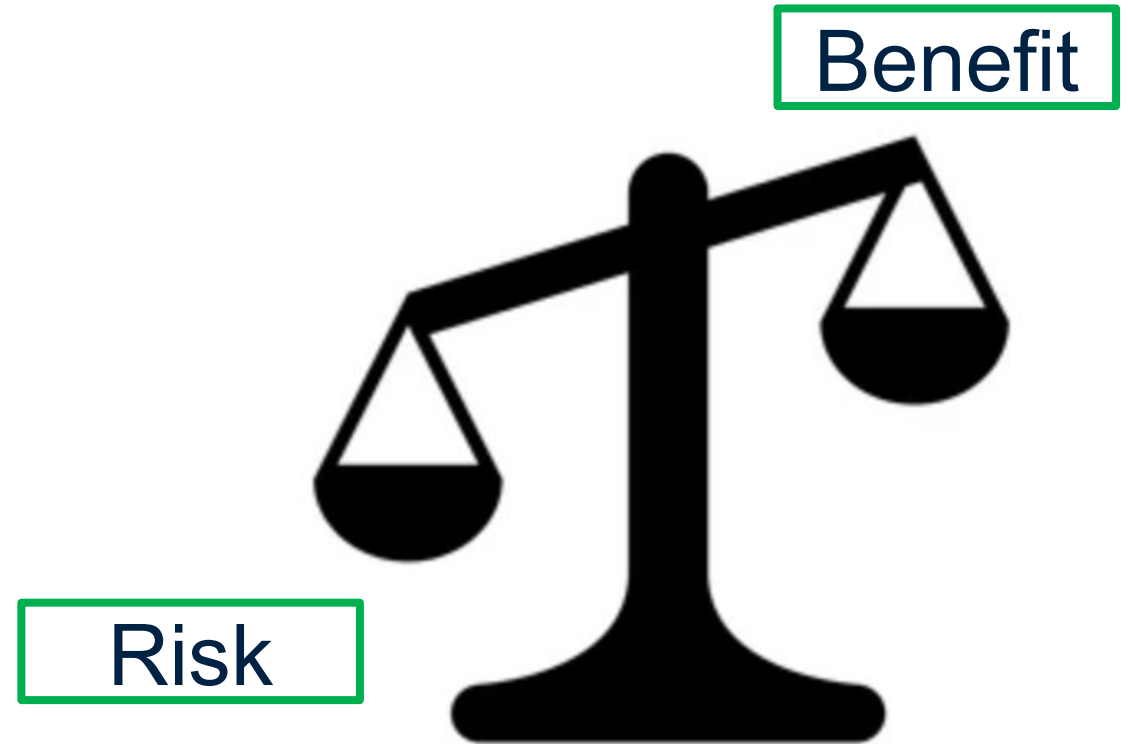
Cancer Free

# 3 Adjuvant therapy options are in use for melanoma

- ▶ Dabrafenib plus Trametinib (for BRAF mutant melanoma)
- ▶ Nivolumab
- ▶ Pembrolizumab

# How do we decide which patients need adjuvant therapy?

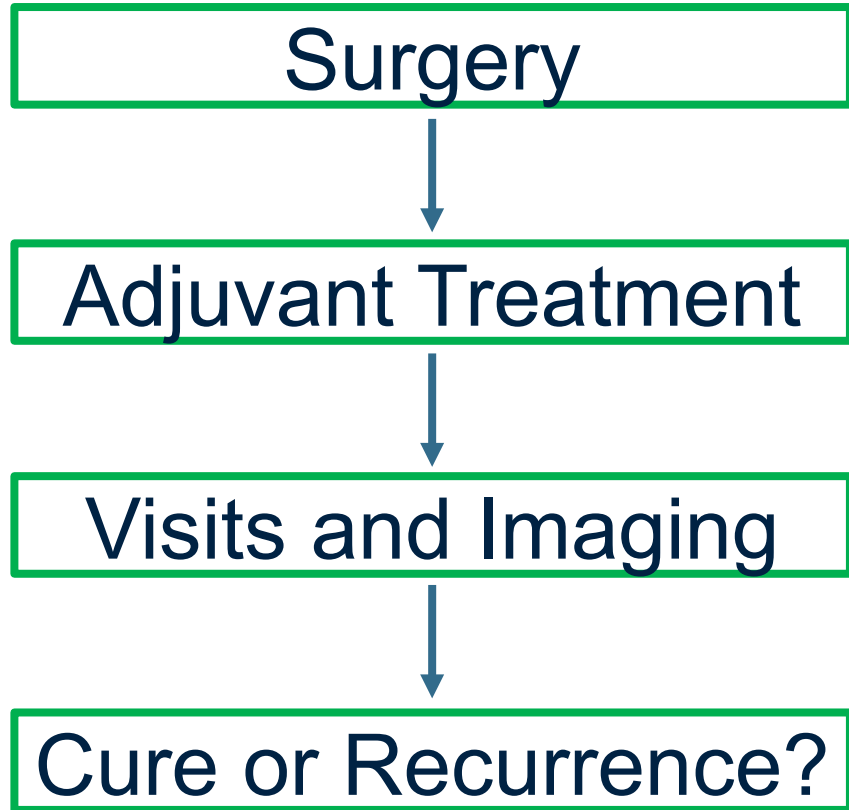
- ▶ What is the risk of cancer recurrence?
  - Low risk → No treatment
  - High risk → Consider treatment
- ▶ What are the risks of the adjuvant treatment?
  - Side effects
  - Time spent travelling to visits and at visits
- ▶ What is the potential benefit of treatment?
  - Improved chance of staying cancer free



# Adjuvant therapy considerations

- ▶ Reduces the risk of recurrence
- ▶ We don't know which patients are benefiting
- ▶ We don't have long term data yet
- ▶ We still need to monitor patients closely for recurrence

# Stage III melanoma, adjuvant therapy approach



# Stage III melanoma, neoadjuvant therapy approach



# A single dose of neoadjuvant PD-1 blockade predicts clinical outcomes in resectable melanoma

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# Neoadjuvant therapy pooled analysis - 2021

- ▶ Data from 6 neoadjuvant trials conducted across the INMC (US, Europe, Australia)
- ▶ Included studies of immunotherapy and BRAF targeted therapy
- ▶ High rate of patients with complete or major pathologic response
- ▶ Patients with complete pathologic responses had higher rates of remaining cancer free
  - For patients treated with immunotherapy, 96% of these patients remain cancer free

# Assessing pathologic response to neoadjuvant therapy



*Annals of Oncology* 29: 1861–1868, 2018  
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## ORIGINAL ARTICLE

### Pathological assessment of resection specimens after neoadjuvant therapy for metastatic melanoma

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# Neoadjuvant therapy recommendations: Consensus from 2 forums

## THE LANCET Oncology

Volume 20, Issue 7, July 2019, Pages e378-e389

Policy Review

### Neoadjuvant systemic therapy in melanoma: recommendations of the International Neoadjuvant Melanoma Consortium

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Reviews

### Neoadjuvant Therapy for Melanoma: A U.S. Food and Drug Administration—Melanoma Research Alliance Public Workshop

# Neoadjuvant clinical trial recommendations

- ▶ Patients with resectable, stage III melanoma involving a lymph node mass
- ▶ Short duration of neoadjuvant treatment before proceeding to surgery
- ▶ Surgical approach follows standard procedures
- ▶ Pathology report should describe and quantify viable tumor and evidence of tumor response
- ▶ Patients still receive adjuvant therapy after surgery to complete up to 1 year

# Potential advantages of neoadjuvant therapy

- ▶ Prognostic value of pathologic response at time of surgery when treatment is given first
  - Convincing data from Penn trial and from our pooled analysis
- ▶ Opportunity to individualize treatment based on pathologic response a time of surgery
  - Limit surgery in patients with a complete pathologic response (Trial ongoing)
  - Limit adjuvant therapy in patients with a complete pathologic response (Trial ongoing)
  - Intensify adjuvant therapy in patients with a pathologic non-response (Trial ongoing)
- ▶ Potential to gain insight into mechanisms of treatment response and resistance
- ▶ Possibility of improved immune response/patient outcomes over adjuvant therapy (Trial ongoing)



# Summary

- ▶ Adjuvant therapy can reduce recurrences in patients with high-risk melanoma
  - Requires a careful and individualized discussion of risks and potential benefit
  - Need longer term data to compare adjuvant therapy versus reserving treatment for recurrence
- ▶ Neoadjuvant therapy is being studied in clinical trials
  - Stage II and stage III neoadjuvant therapy clinical trials ongoing at Penn
- ▶ Pathological responses to neoadjuvant therapy are prognostic of decreased recurrence
  - We know which patients are benefitting
  - More importantly, we know which patients may not be benefitting and that is how we start to improve outcomes in patients with high-risk melanoma
- ▶ Ongoing trials will further define the role of neoadjuvant therapy, and the indications for limiting surgery and adjuvant therapy in patients with major pathological responses

