
Global Resource for Advancing Cancer Education

# What is the value of maintenance therapy in advanced NSCLC, and who should get it?

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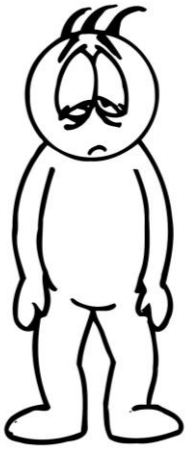
# Why Maintenance Therapy?

- The concept of delivering maintenance therapy is based on several basic concepts in managing advanced non-small cell lung cancer (NSCLC).



- First line treatment is effective in shrinking cancer or controlling (keeping cancer stable) in many patients
- Continuing standard first line treatment with combination chemotherapy (most common first line treatment) is usually infeasible due to cumulative toxicity…neuropathy, fatigue, etc.
- Maintenance therapy is the concept that you can “maintain” a good response with a sustainably tolerable cancer treatment that is effective enough to continue to control the cancer after a “best response” has already been induced to first line therapy.

# "Down-Shifting" to a Less Challenging but Still Effective Therapy

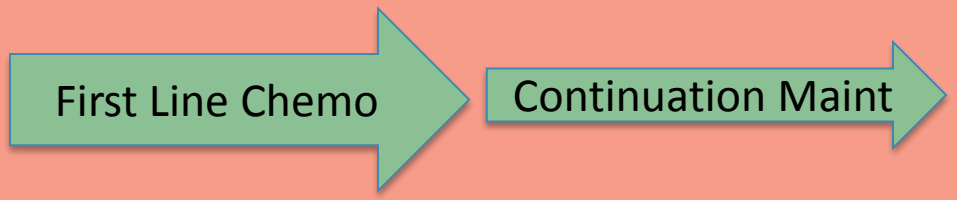
***downshift (noun)***

to reduce the speed, rate or intensity; to simplify commitments in life

## Two Basic Mechanisms

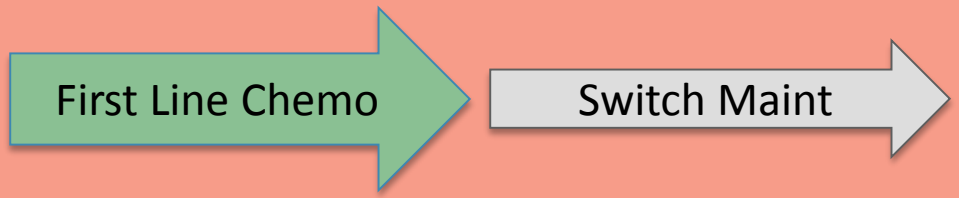
(neither proven better or worse)

*"Continuation" maintenance*:
after 4-6 cycles 1st line, drop >1 drug, keep others going until progression




*Both approaches less intensive than first line combo therapy*

*"Switch" maintenance*:
after 4-6 cycles 1st line, stop all, switch directly to new drug(s)

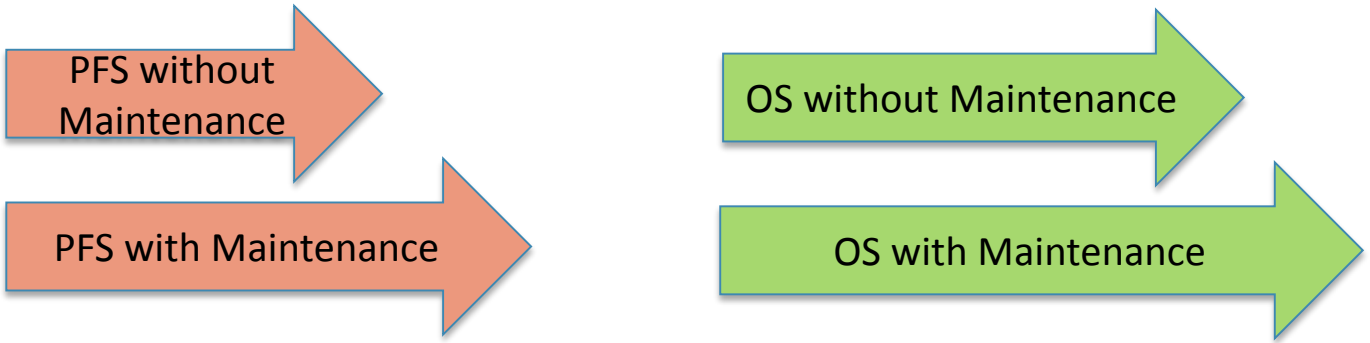


# What agent(s)?

- The agents that have been tested and demonstrated significant success have been those that had already been shown to improve survival in patients with previously treated advanced NSCLC (after prior progression)
  - Taxotere (docetaxel)
  - Alimta (pemetrexed)
    - Avastin (bevacizumab sometimes added)
  - Tarceva (erlotinib)
  - Avastin alone is sometimes used, its value never directly tested
- People starting on oral targeted therapies (EGFR or ALK inhibitors) generally continue these until progression (essentially continuation maintenance therapy)
- No option proven better than another.

# Why Maintenance?

- Studies with these agents have demonstrated consistent improvement in progression-free survival (PFS) (time before cancer begins to grow)
- Trials with Alimta or Tarceva have demonstrated a statistically significant overall survival (OS) benefit in favor of maintenance.
- Comparable benefits have been seen with either a "continuation" (with Alimta +/- Avastin, sometimes Avastin alone) or "switch" maintenance therapy (with Alimta or Tarceva)

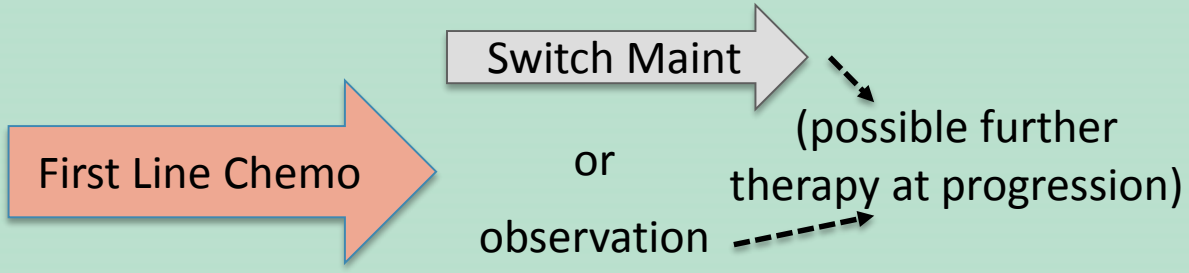


# Wherefore Taxotere?


- The recognition that maintenance therapy could be valuable actually started with Taxotere also shows very clear improvement in PFS, not clinically significant but still notable trend of better OS (about 2.5 mo!)
- Why is Taxotere rarely considered as a maintenance therapy for advanced NSCLC?
  - The key trial with it was underpowered to show a significant survival benefit?
  - Its side effect profile makes it challenging to continue longitudinally
  - Nobody is marketing Taxotere anymore

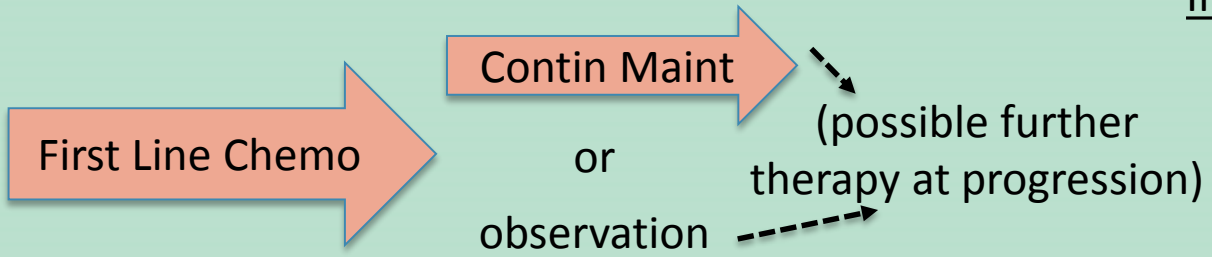
# Why NOT Maintenance?

- While maintenance therapy definitely improves PFS, the studies that show a survival benefit with maintenance therapy all had major imbalance favoring maintenance therapy arm.




Imbalance in Switch Maintenance

100% got effective therapy after first line
vs.
~20% got effective therapy after first line




Imbalance in Contin Maintenance

Contin maint therapy arm gets far more of an effective therapy than obs arm

# What does the Imbalance Mean??

- The trials that support maintenance therapy have shown a few points clearly:
  - The agents that are effective in second line are affirmed as improving survival in maintenance therapy
  - The patients who didn't progress first line (those eligible for maintenance) are the ones most likely to benefit from further therapy
  - In patients who have not progressed after 4 cycles of first line chemo, you do not exhaust the benefit of Alimta (and possibly other chemo agents, but not demonstrated) after 4 cycles.
- These trials do NOT show that subsequent treatment must be given as maintenance therapy. They show that patients who respond to initial treatment benefit from MORE therapy after first line and should get it.
- Maintenance therapy is the way to ensure that further treatment is administered.

# So Should Everyone Eligible Get Maintenance Therapy for Advanced NSCLC?

- Maintenance therapy is the surefire way to ensure that people who haven't progressed get subsequent effective therapy.
- But that doesn't mean that everyone needs it. Who doesn't?

- People who really need a break because of fatigue or planned holiday off or just because, honestly, they don't owe an explanation.
- People who have had a very good response and/or have indolent disease, in whom you can rightly feel confident you'll have time to start chemo after progression without missing the opportunity.

- **The decision on maintenance therapy should be individualized.**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