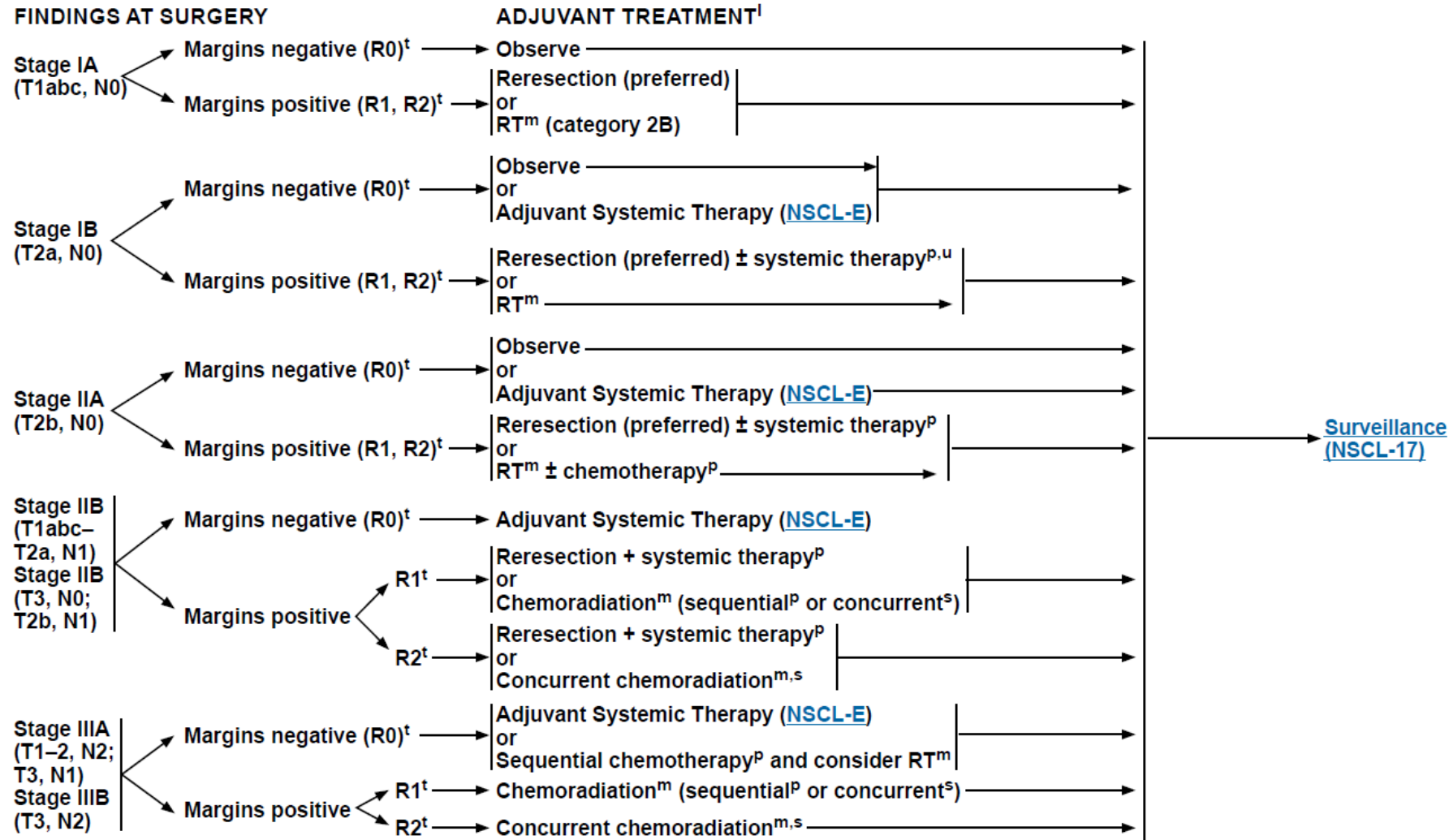


NSCLC – záplava léčebných možností aneb co nás čeká v personalizované léčbě nádorů plic x hrazené možnosti léčby

Jindřich Fínek

Jihočeské onkologické dny 2024



Footnotes, [NSCL-4A](#)

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

Nemalobuněčný karcinom plic (NSCLC): negeralizovaná stadia

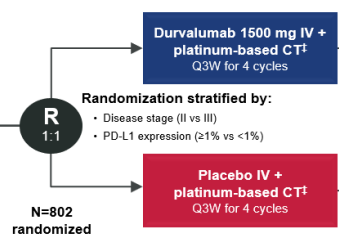
- **Stadium I** -> chirurgická léčba (+ příp. reresekce v případě R1 nebo R2)
 - IB s vysokým rizikem recidivy (např. angioinvasze, invaze pleury, klínová resekce a pNX) -> adjuvance CHT
 - IB EGFRm po úplné resekcii -> **adjuvance osimertinib** (ADAURA)
- **Stadium II** -> chirurgická léčba (+ příp. reresekce v případě R1 nebo R2)
 - Vysoké riziko recidivy & PD-L1 $\geq 1\%$: **neoadjuvance nivolumab** s CHT (Pt) (CheckMate 816)
 - EGFR & ALK neg. & PD-L1 $\geq 50\%$ & vysoké riziko recidivy po R0 resekcii a CHT (Pt) -> **adjuvance atezolizumab** (IMPower010)
 - EGFRm po úplné resekcii -> **adjuvance osimertinib** (ADAURA)
- **Stadium IIIA** -> chirurgická léčba
 - Neoadjuvance CHT (Pt) / cCRT (Pancoast)
 - Vysoké riziko recidivy & PD-L1 $\geq 1\%$: **neoadjuvance nivolumab** s CHT (Pt) (CheckMate 816)
 - Adjuvance CHT (Pt) / RT
 - EGFR & ALK neg. s vysokým rizikem recidivy, po R0 resekcii a CHT (Pt), PD-L1 $\geq 50\%$ -> **adjuvance atezolizumab** (IMPower010)
 - EGFRm -> **adjuvance osimertinib** (ADAURA)
- **Stadium IIIA a IIIB inoperabilní (IIIC ... 8 edice AJCC)**
 - cCRT / sCRT / RT
 - EGFR & ALK neg. & PD-L1 $\geq 1\%$ bez progresu po CRT (Pt) -> **durvalumab** (PACIFIC) ... **po konkomitantní CRT**
 - EGFRm -> **osimertinib** (FLAURA), **erlotinib**, **gefitinib**, **afatinib**
 - KRAS (G12C) -> **sotorasib**, a další viz. cílená léčba u stadia IV ...

Perioperační podání imuno / cílené léčby: v přípravě

AEGEAN: a phase 3, global, randomized, double-blind study

Study population

- Treatment-naïve
- ECOG PS 0 or 1
- Resectable NSCLC* (stage IIA–IIIB[N2]; AJCC 8th ed)
- Lobectomy, sleeve resection, or bilobectomy as planned surgery*
- Confirmed PD-L1 status†
- No documented EGFR/ALK aberrations*



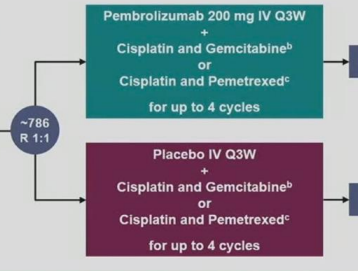
KEYNOTE-671 Study Design Randomized, Double-Blind, Phase 3 Trial

Key Eligibility Criteria

- Pathologically confirmed, resectable stage II, IIIA, or IIIB (N2) NSCLC per AJCC v8
- No prior therapy
- Able to undergo surgery
- Provision of tumor sample for PD-L1 evaluation*
- ECOG PS 0 or 1

Stratification Factors

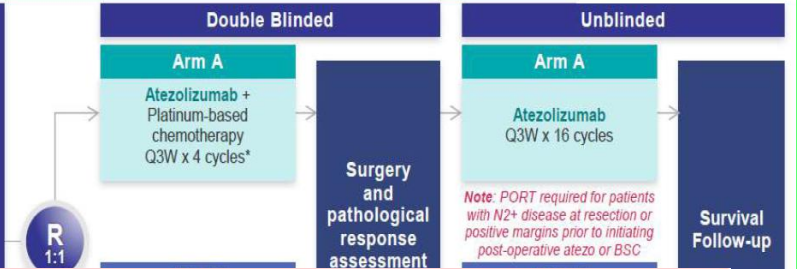
- Disease stage (II vs III)
- PD-L1 TPS* (<50% vs ≥50%)
- Histology (squamous vs nonsquamous)
- Geographic region (east vs west)



IMpower030 Neoadjuvant Atezolizumab + Platinum-based Chemotherapy

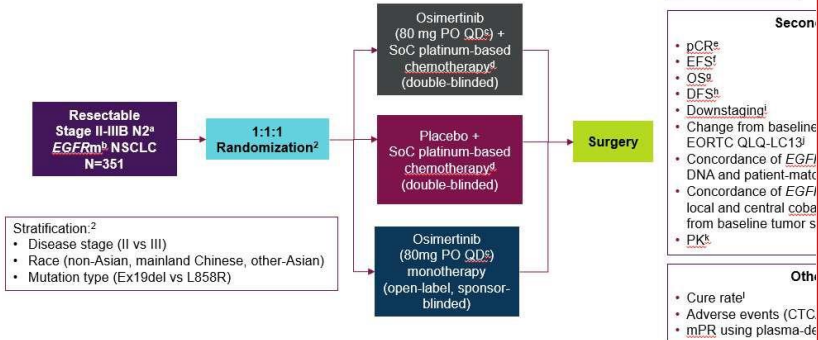
Resectable Stage II, IIIA, or select IIIB (T3N2) NSCLC
ECOG PS 0–1
ALK-/EGFR- (NSQ only)
N=302

Stratification



NeoADAURA: Study Design

Phase III, randomized, multicenter study¹



- Stratification:²
- Disease stage (II vs III)
 - Race (non-Asian, mainland Chinese, other-Asian)
 - Mutation type (Ex19del vs L858R)

Primary endpoint

- mPR³

Secondary endpoint

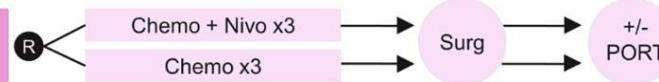
- pCR⁴
- EFS⁵
- OS⁶
- DFS⁷
- Downstaging⁸
- Change from baseline EORTC QLQ-LC13⁹
- Concordance of EGFR DNA and patient-matched tumor¹⁰
- Concordance of EGFR local and central copy from baseline tumor sample¹¹
- PK¹²

Other endpoints

- Cure rate¹³
- Adverse events (CTC grade 3/4)
- mPR using plasma-derived samples¹⁴

¹Classified according to the 8th edition of AJCC staging classification. ²Ex19del and/or L858R. ³Dose may be reduced to 40 mg PO QD at the discretion of the investigator's choice: cisplatin/pemetrexed, or carboplatin/pemetrexed. ⁴From date of randomization to an average of 12 weeks after the first dose. ⁵Up to approximately 15 months after the last patient is randomized. ⁶Up to approximately 5.5 years after the last patient is randomized. ⁷From date of randomization to approximately 15 months after the last patient is randomized. ⁸From date of randomization to an average of 12 weeks after the first dose. ⁹From randomization to 24 weeks post-surgery. ¹⁰From the pre-dose of Cycle 2 to post-dose of Cycle 2 (21 days). ¹¹From the surgery until five years after surgery. ¹²From randomization to Week 264 post-surgery. ¹³From randomization to Week 264 post-surgery. ¹⁴From randomization to Week 264 post-surgery.

Checkmate 816¹
n=358
Stage IB-III

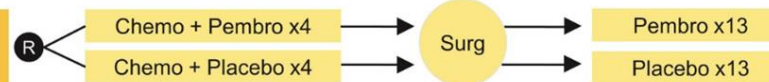


Primary Endpoint(s)

pCR, EFS

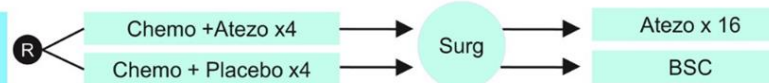
¹Checkmate 77T is a similar study that includes 1 year of adjuvant nivolumab

KEYNOTE 671
n=786
Stage II-III



EFS, OS

IMpower030
n=450
Stage II-III



EFS

AEGEAN
n=800
Stage II-III



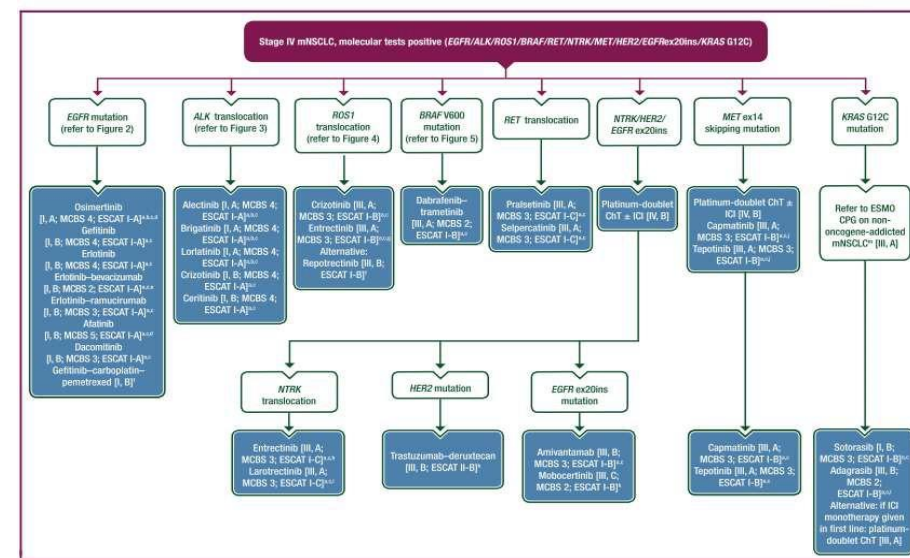
pCR, EFS

NSCLC: stadium IV, bez řídící mutace

- Bez ohledu na PD-L1 expresi
 - PS 0-1: chemo-imunoterapie
 - Neskvamózní: pembrolizumab+pemetrexed+Pt, atezolizumab+bevacizumab+karboplatina+paklitaxel, atezolizumab+karboplatina+nabpaklitaxel, nivolumab+ipilimumab+Pt, durvalumab+tremelimumab+Pt
 - Skvamózní: pembrolizumab+karboplatina+paklitaxel/nab-paklitaxel, nivolumab+ipilimumab+Pt, durvalumab+tremelimumab+Pt
 - PS 0-2: chemoterapie
 - Neskvamózní: pemetrexed+Pt, karboplatina+/-cytostatikum 3. generace, bevacizumab+cytostatikum+Pt)
 - Skvamózní: karboplatina+/-cytostatikum 3. generace, Pt+cytostatikum 3. generace
- PD-L1 \geq 50 %, skvamózní i neskvamózní: imuno-monoterapie (pembrolizumab, atezolizumab, cemiplimab)

NSCLC: stadium IV, s řídicí mutací

- EGFR: osimertinib (+ CHT) – afatinib – erlotinib (+ udržovací léčba) – erlotinib+bevacizumab – gefitinib – dacomitinib – amivantamab + lazertinib
- ALK: alectinib – brigatinib – ceritinib – crizotinib – lorlatinib
- ROS1: entrectinib – crizotinib
- BRAF: dabrafenib/ trametinib
- NTRK: entrectinib – larotrectinib
- RET: pralsetinib – seliperkatinib (po předchozí CIT)
- KRAS: sotorasib – adagrasib (G12C, po předchozí systémové léčbě)
- MET: tepotinib (po předchozí CIT) / capmatinib (po předchozí CIT)
- HER2: trastuzumab-deruxtecan (po předchozí systémové léčbě - EMA)
- BRAF: dabrafenib + trametinib



Druhá a další linie léčby u EGFR (nebo ALK) mutovaných NSCLC

- T790M+ -> osimertinib (AURA3)
- T790M- -> CHT (Pt) / atezolizumab (s bevacizumabem a CHT) nebo pembrolizumab (PD-L1 ≥ 1 %) / erlotinib nebo afatinib ve 3. linii, pokud nebyly použity dříve
- Inzerce exon 20 : amivantamab po selhání CHT (Pt)

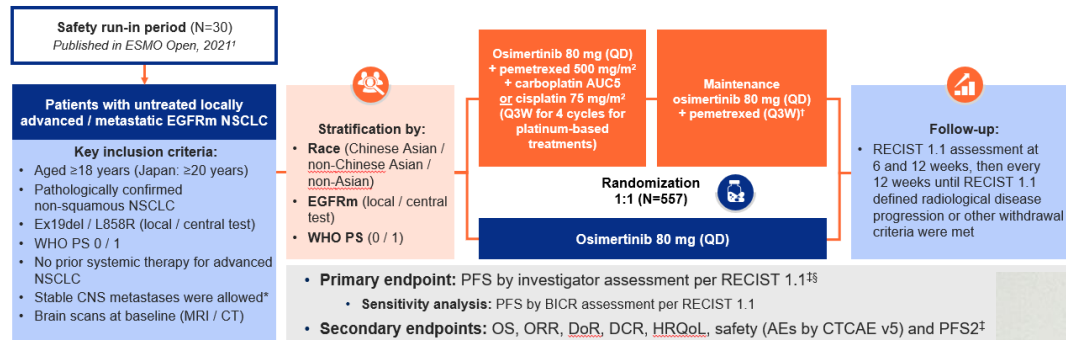
hrazeno

nehrazeno

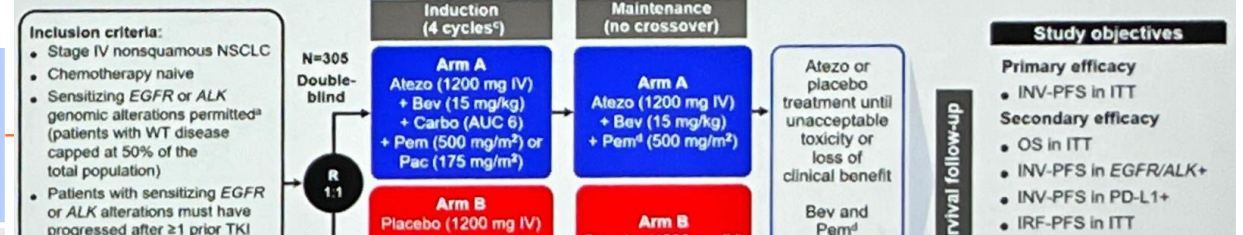
neregistrováno

Co do budoucna: Intenzivnější režim? Léčba při rezistenci na cílenou terapii ... TKI / CIT? Markery?

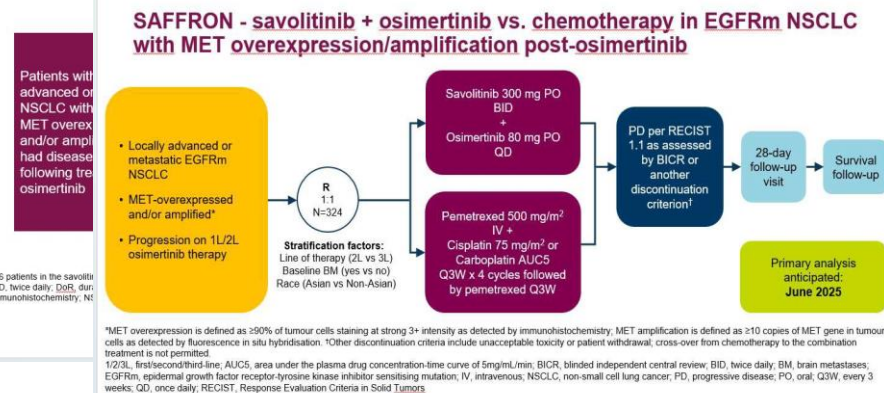
FLAURA2 Phase III study design



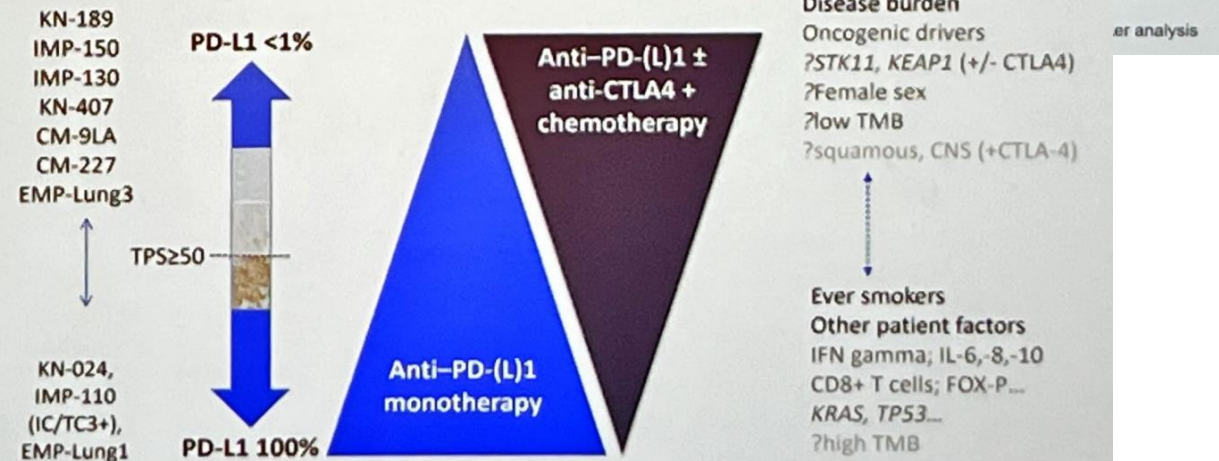
IMpower151 study design



SAVANNAH – savolitinib+osimertinib in EGFRm NSCLC Post-osimertinib: design studie fáze II



How do we choose?

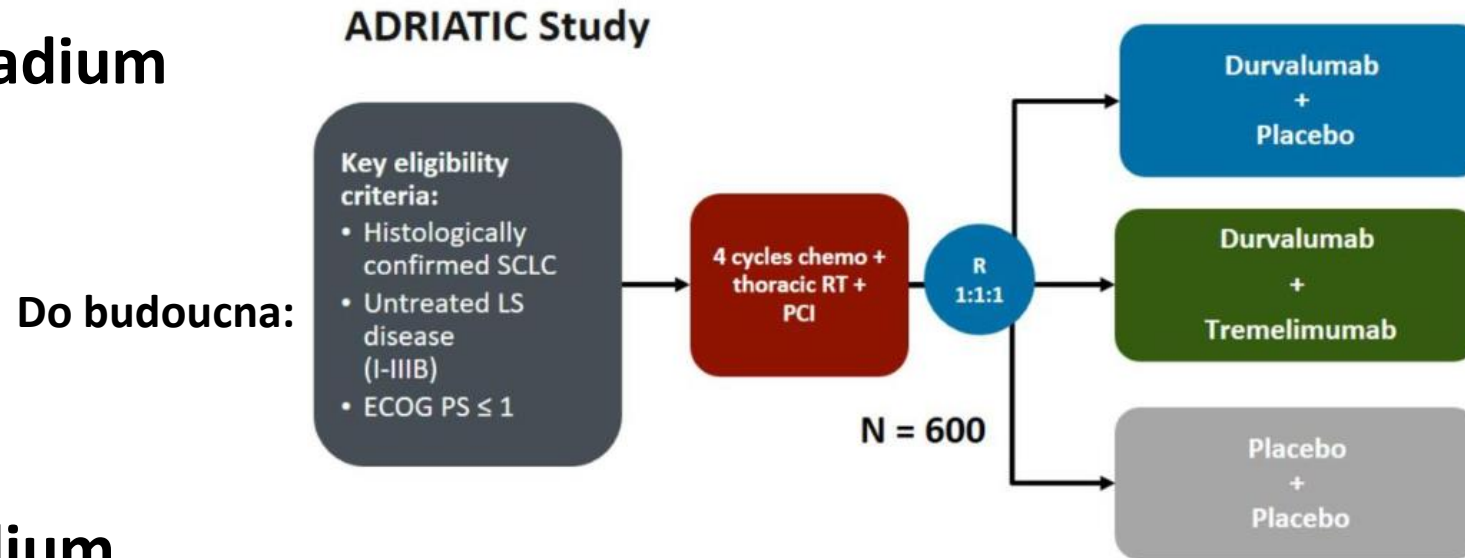


Li S. SAFFRON: Ph3 savolitinib + osimertinib vs chemotherapy in EGFRm NSCLC with MET overexpression/amplification post-osimertinib. #EP19.02-138, IASLC 2022 World Conference on Lung Cancer, Vienna, Austria

Malobuněčný karcinom plic (SCLC)

- **Limitované stadium**

- etoposid+Pt



- **Pokročilé stadium**

- **durvalumab**+etoposid+Pt (karbo / cisplatina)
- **atezolizumab**+etoposid+karboplatina
- **Budoucnost ?**
 - DeLLphi-301 - **tarlatamab**
 - ETER701 - **benmelstobart**

hrazeno

nehrazeno

neregistrováno



Děkuji za pozornost