Dr. Rasna Gupta

Dr. Rasna Gupta is an Assistant Professor and the lead of the Peer Support and Physician Wellness Program at the Windsor Campus, Schulich School of Medicine and Dentistry, Western University, London, ON. She is also an adjunct professor at University of Windsor. She has been with Windsor Regional Hospital since 2011 and has clinical interest in Breast cancer, Lung cancer, GIST and a variety of Hematologic malignancies.

Dr. Gupta enjoys teaching and is the Oncology Lead for the Undergraduate Clinical Teaching Unit and has received rewards for her work. She also serves as the program lead for Clinician Wellness Program at the Windsor Regional Cancer Centre, is a member of the City Wide Ethics and Credentialing Committee, and is a member of the Physician Recruitment and Retention Committee at Windsor Regional Hospital. Dr. Gupta has been a local Lead for breast cancer at the NCIC Breast Cancer Committee and a member of Provincial Breast Cancer Guidelines Committee with Cancer Care Ontario. She serves as a Regional Lead for Oncology for Windsor Regional Cancer Centre.

Dr. Gupta is also the member for guidelines committee Provincial Hematology disease site group. She has helped author multiple guidelines and has been involved with other practice improving initiatives for Cancer Care Ontario. She is currently working on making guidelines at both local and provincial level for delivery of bispecific antibodies. She also works at CPSO as a Peer assessor and is responsible for conducting peer assessment based on age or referral from quality program as well as the Registration assessments.

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CANCER EDUCATION DAY

The Decision Between Surgery, Chemotherapy and Radiation

Dr. Rasna Gupta

December 13, 2024

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Presenter Disclosure

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Early-Stage NSCLC – Learning Objectives:

- Create strategies for the use of neoadjuvant therapy in patients with early NSCLC, personalizing therapy selection according to evidence, expert recommendations, and individual patient factors
- Evaluate evidence for the role of individual patient and tumor characteristics for the use of adjuvant therapy in patients with resected NSCLC
- Define perioperative therapy in early NSCLC and its potential application and benefits

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RFS rates after surgery for NSCLC by stage

Recurrence rates for stage II NSCLC

- 3-yr: 42%
- 5-yr: 50%

Recurrence rates for stage III NSCLC

- 3-yr: 62%
- 5-yr:

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Shift to Neoadjuvant Treatment With Chemotherapy plus Immunotherapy

- Historically, did not do much neoadjuvant chemotherapy alone
- Adjuvant chemotherapy alone offered modest benefit
- Then, trials adding immunotherapy in adjuvant setting demonstrated improved outcomes
- Shift now to neoadjuvant chemotherapy plus immunotherapy
  - But what does that mean for biomarker positive disease?

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PDL1 expression in Early Stage NSCLC

- In the metastatic setting, PD-L1 positivity is predictive for response to single-agent immunotherapy
- Currently, immunotherapy drugs are approved in both adjuvant and neoadjuvant settings
- Outcomes with immunotherapy are generally more favorable in groups with high PD-L1 expression or at least some level of PD-L1 expression. So adjuvant immunetherapy is standard of care in patients with PDL1 more than 50%.

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Targeted Therapies Approved in Adjuvant setting

- **Osimertinib**: approved as adjuvant therapy after tumor resection in patients with NSCLC whose tumors have *EGFR* exon 19 deletions or exon 21 L858R mutations
  - Once daily oral dosing for up to 3 yr
  - Prior platinum-based adjuvant chemotherapy allowed in ADAURA
- **Alectinib**: approved as adjuvant treatment in patients following tumor resection of ALK-positive NSCLC (tumors ≥4 cm or node positive)
  - Twice daily oral dosing for up to 2 yr
  - No prior adjuvant chemotherapy in ALINA
- No targeted therapies approved in the neoadjuvant setting

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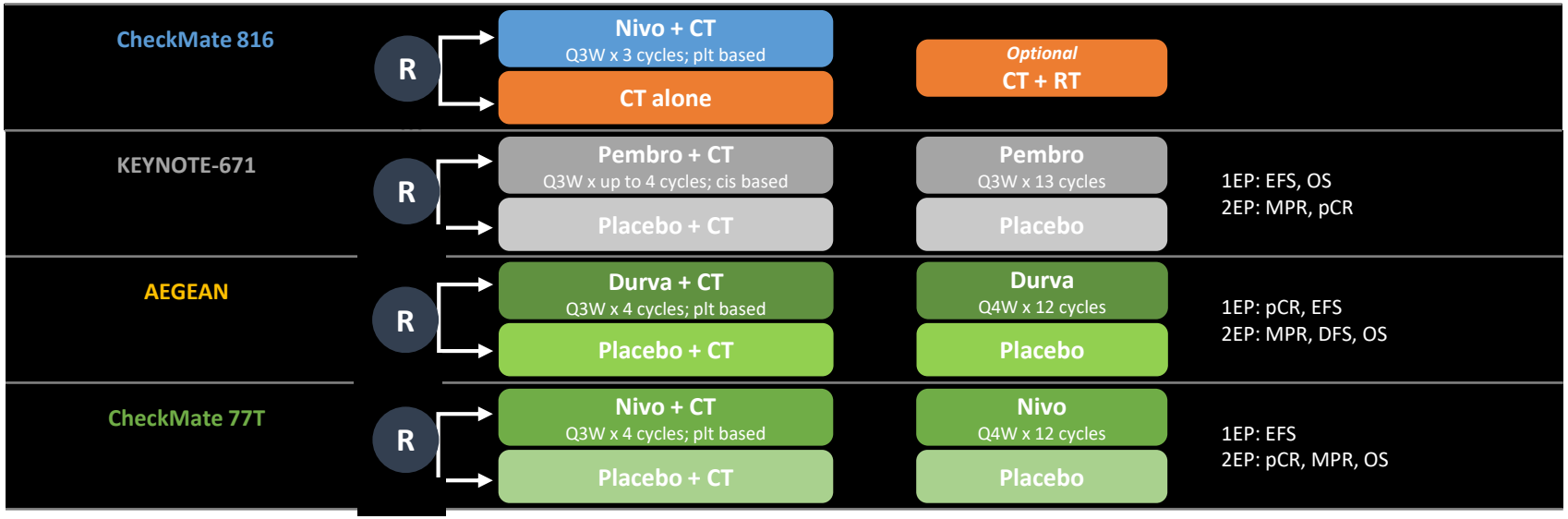
Key Trials With Neoadjuvant Chemotherapy Plus Immunotherapy



Forde. NEJM. 2022;386:1973. Wakelee. NEJM. 2023;389:491. Heymach. NEJM. 2023;389:1672.
Cascone. NEJM. 2024;390:1756.

Neoadjuvant and Perioperative IO Trials

Trial	CheckMate 816[1,2]		KEYNOTE-671[3-5]		AEGEAN[6,7]		CheckMate 77T[8,9]	
Neoadjuvant therapy	Nivo + CT, 3 cycles	CT alone, 3 cycles	Pembro + CT, 4 cycles	Placebo + CT, 4 cycles	Durva + CT, 4 cycles	Placebo + CT, 4 cycles	Nivo + CT, 4 cycles	Placebo + CT, 4 cycles
Adjuvant therapy	Optional CT, 4 cycles	Optional CT, 4 cycles	Pembro, 13 cycles	Placebo, 13 cycles	Durva, 12 cycles	Placebo, 12 cycles	Nivo, 12 cycles, Q4W	Placebo, 12 cycles, Q4W
CT regimens	Carboplatin or cisplatin; Cisplatin in CT-only arm		Cisplatin		Cisplatin or carboplatin		Cisplatin or carboplatin	
Nodal status: N0/N1/N2, %	Not reported		37.3/20.4/42.3	35.5/17.8/46.8	30.1/20.5/49.5	27.3/23.3/49.5	Not reported	
pCR, %	**24.0**	**2.2**	**18.1**	**4.0**	**17.2**	**4.3**	**25.3**	**4.7**
Completed surgery	83.2	75.4	82.1	79.4	77.6	76.7	77.7	76.7
Median f/u, mo	57.6		36.6 (range: 18.8-62.0)		25.9 (range: 0-56.6)		33.3 (range: 23.6-52.1)	
mEFS, mo (95% CI)	**43.8**	**18.4**	**47.2 (32.9-NR)**	**18.3 (14.8-22.1)**	**NR (42.3-NR)**	**30.0 (20.6-NR)**	**40.1 (33.7-NR)**	**17.0 (13.6-28.1)**
HR for mEFS	0.66 (0.49-0.90)		0.59 (0.48-0.72)		0.69 (0.53-0.88)		0.59 (0.45-0.79)	
mOS, mo (95% CI)	**NR**	**NR**	**NR (NR-NR)**	**52.4 (45.7-NR)**	**NR**	**53.2 (44.3-NR)**	**Not yet tested**	
HR for mOS	0.71 (98.36% CI, 0.47-1.07)		0.72 (0.56-0.93)		0.89 (0.70-1.14)		N/A	

1. Forde. NEJM. 2022;386:1973. 2. Spicer. ASCO 2024. Abstr LBA8010. 3. Wakelee. ASCO 2023. Abstr LBA100. 4. Wakelee. NEJM. 2023;389:491. 5. Spicer. ESMO 2023. Abstr LBA56. 6. Heymach. WCLC 2024. Abstr OA13.03. 7. Heymach. NEJM. 2023;389:1672. 8. Spicer. ESMO 2024. Abstr LBA50. 9. Cascone. NEJM. 2024;390:1756.

Immunotherapy Approvals for Neoadjuvant and Adjuvant Therapies in Early-Stage NSCLC

Neoadjuvant	Perioperative	Adjuvant
Nivolumab: combined with plt-based CT, adults with resectable NSCLC (CheckMate 816 trial)	**Durvalumab:** for resectable NSCLC (tumors ≥4 cm or node positive) combined with plt-based CT; continued as single agent after surgery (AEGEAN trial) **Pembrolizumab**: for resectable NSCLC (tumors ≥4 cm or node positive) combined with plt-based CT; continued as single agent after surgery (KEYNOTE-671 trial) **Nivolumab**: for resectable (tumors ≥4 cm and/or node positive) NSCLC combined with plt-doublet CT; continued as single agent after surgery (Checkmate 77T trial)	**Atezolizumab:** following resection and plt-based CT, adults with stage II-IIIA and PD-L1 ≥1% of tumor cells (IMpower010 trial) **Pembrolizumab:** Following resection and plt-based CT, adults with stage IB-IIIA (KEYNOTE-091 trial)

Atezolizumab PI. Durvalumab PI. Nivolumab PI. Pembrolizumab PI.

Key Takeaways for IO in Resectable Nonmetastatic NSCLC

- Immune checkpoint blockade has become a standard of care for the curative intent treatment of multiple tumor types
- Incorporation of novel systemic therapies in the perioperative period necessitates team working across medical and surgical specialties
- Choice among neoadjuvant, adjuvant, or perioperative strategies should be individualized to the patient and the patient's tumor-specific characteristics
- Multiple randomized phase III trials demonstrate superiority of neoadjuvant/perioperative chemotherapy-IO vs chemo alone
- OS is the gold standard for demonstrating benefit of adjuvant therapy

Key Takeaways for IO in Resectable Nonmetastatic NSCLC

- Neoadjuvant chemo-IO is a SoC for surgically resectable NSCLC; given OS benefit in KEYNOTE-671 perioperative chemo-IO should be standard
- Patients with a pCR have significantly longer OS and EFS than those who had an incomplete or major pathologic response at time of resection
- Atezolizumab (PD-L1 ≥1%) and pembrolizumab (all PD-L1 expression levels) are now approved adjuvant therapies in stage II-IIIA and stage IB-IIIA NSCLC, respectively
  - Recommend adjuvant anti–PD-1 in tumors PD-L1 ≥50% and have conversation around pros/cons in patients with PD-L1 1%-49% and use in select circumstances
- Need more data on PD-L1–negative patients and node-negative tumors
- Need more data on biomarkers (eg, ctDNA) to help guide decisions

Question & Answer