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Positive Quality Intervention: Durvalumab (Imfinzi®) Therapy Overview in Non-Small Cell Lung Cancer (NSCLC) and Small Cell Lung Cancer (SCLC)

Description: This PQI addresses the management of durvalumab and immune-mediated adverse events in treating Stage III unresectable non-small cell lung cancer (NSCLC) and first-line extensive-stage small cell lung cancer (ES-SCLC).

Background: Durvalumab is a monoclonal antibody that inhibits PD-L1 and is indicated for use in:[1]

- **NSCLC:**
  - Resectable NSCLC (without EGFR mutations or ALK rearrangements): in combination with platinum-based chemotherapy as neoadjuvant treatment, followed by durvalumab monotherapy as adjuvant therapy
  - Unresectable Stage III NSCLC: as a single agent for patients whose disease has not progressed after concurrent platinum-based chemotherapy and radiation
  - Metastatic NSCLC (without EGFR mutations or ALK aberrations): combined with tremelimumab-actl and platinum-based chemotherapy
- **SCLC:**
  - Limited-stage: As a single agent in patients whose disease has not progressed after concurrent platinum-based chemotherapy and radiation
  - Extensive-stage: Combined with etoposide and carboplatin or cisplatin as first-line treatment
- Additional indications – see prescribing information[1]

Most common adverse reactions (≥ 20%) in lung cancer:[1]

- Single agent (unresectable Stage III): cough, fatigue, pneumonitis/radiation pneumonitis, upper respiratory infections, dyspnea, and rash
- Combined with platinum-based chemotherapy (ES-SCLC): nausea, fatigue/asthenia, and alopecia

PQI Process: Upon order of durvalumab[1]

- Verify dosing of durvalumab as an intravenous infusion over 60 minutes
  - Stage III NSCLC
    - Weight 30 kg and more: 10 mg/kg every 2 weeks or 1500 mg every 4 weeks
    - Weight < 30 kg: 10 mg/kg every 2 weeks
  - Extensive-Stage small cell lung cancer (ES-SCLC)
    - Weight > 30kg: 1500 mg every 3 weeks in combination with chemotherapy for 4 cycles, then 1500 mg every 4 weeks as a single agent
    - Weight < 30kg: 20 mg/kg every 3 weeks in combination with chemotherapy for 4 cycles, then 10 mg/kg every 2 weeks as a single agent
- Durvalumab comes in both 500 mg/10mL and 120 mg/2.4 mL (both 50 mg/mL) single-dose vials
- Withdraw the required volume from the vial(s) and transfer into intravenous bag containing 0.9% Sodium Chloride or 5% Dextrose, mixing diluted solution by gentle inversion (do NOT shake)
  - Final concentration should be between 1 mg/mL-15 mg/mL
- Administer intravenously over 60 minutes through line containing a sterile, low-protein binding 0.2 or 0.22 micron in-line filter
- Follow the table below for guidelines regarding immune related adverse reaction/events, dosage

reduction is not recommended[1]

irAE	Withhold Durvalumab	Discontinue Durvalumab	Steroids
Pneumonitis	Grade 2*	Grade 3 or 4	Grade 2: Initial dose of 1–2 mg/kg/day prednisone or equivalent followed by a taper Grade 3 or 4: Initial dose of 1–2 mg/kg/day prednisone or equivalent followed by a taper
Colitis	Grade 2 or 3*	Grade 4	Grade 2, 3, 4: Initial dose of 1-2 mg/kg/day prednisone or equivalent followed by a taper
Hepatitis with no tumor involvement of the liver	ALT or AST > 3 and up to 8x ULN* Or total bilirubin 1.5 and up to 3x ULN*	ALT or AST >8x ULN Or Total Bilirubin >3x ULN	Grade 2, 3, 4: Initial dose of 1-2 mg/kg/day prednisone or equivalent followed by a taper
Hepatitis with tumor involvement of the liver	ALT/AST at baseline >1 and up to 3x ULN and increase to >5 and up to 10x ULN* Or ALT/AST at baseline >3 and up to 5x ULN and increase to >8 and up to 10x ULN*	ALT or AST >10x ULN Or Total Bilirubin >3x ULN	
General Guidance	Grade 3 irAE	Grade 4 irAE or recurrent Grade 3 irAE: Discontinue if complete/partial resolution does not occur or unable to reduce steroid dose to 10 mg or less of prednisone or equivalent per day within 12 weeks	For other irAE: Grade 4: Initial dose of 1–2 mg/kg/day prednisone or equivalent followed by a taper
Endocrinopathies	Grade 3 or 4 withhold until stable	Grade 3 or 4: permanently discontinue depending on severity	Adrenal insufficiency hypophysitis/hypopituitarism Grades 2,3,4: Initiate 1–2 mg/kg/day prednisone or equivalent followed by a taper and hormone replacement as indicated
Nephritis with renal dysfunction	Grade 2 or 3 increased blood creatinine*	Grade 4 increased blood creatinine	Grade 2,3,4: Initial dose of 1–2 mg/kg/day prednisone or equivalent followed by a taper
SJS, TEN, or DRESS	Suspected	Confirmed	Grade 2,3,4: Initial dose of 1-2 mg/kg/day prednisone or equivalent followed by a taper
Myocarditis	N/A	Grade 2, 3, or 4	
Neurological Toxicities	Grade 2*	Grade 3 or 4	
Infusion Related Reaction	Grade 1, 2: Interrupt/slow rate of infusion and consider using pre-medications with subsequent doses	Grade 3 or 4	

* Resume durvalumab in patients with complete or partial resolution (Grade 0 or 1) after corticosteroid taper[5,6]

- Additional Adverse Event Management
    - Reactions occurring for All Grades include cough (40%), pneumonitis (34%), dyspnea (25%), fatigue (34%), upper respiratory infections (26%), and rash (23%) with 15% discontinuation rate

due to adverse reactions
    - Consider use of irAE Assessment Tool

Patient-Centered Activities:

- Provide Intravenous Cancer Treatment Education (IVE) Sheet
- Counsel patient on irAE symptoms and when to report symptoms to oncologist
- Schedule regular visits for blood tests (CBC, renal, hepatic, pancreatic, thyroid) and monitoring
- Consider early initiation of steroids as necessary
- Imfinzi® Nurse Center available
    - Nurse Symptom Tracker, imAR Handbook, Wallet Card, Patient Brochures, Dosing Guide, App
- Patient Assistance: NCODA Financial Assistance Tool

References:

1. Imfinzi (durvalumab) [prescribing information]. Wilmington, DE. AstraZeneca Pharmaceuticals LP.
2. Antonia SJ, Villegas A, Daniel D, et al; for the PACIFIC Investigators. Overall Survival with Durvalumab after Chemoradiotherapy in Stage III NSCLC. *N Engl J Med*. 2018;379:2342-2350.
3. Faivre-Finn C, Vicente D, Kurata T, et al. Durvalumab after chemoradiotherapy in stage III NSCLC: 4-year survival update from the phase 3 PACIFIC trial. Presented at: 2020 ESMO Virtual Congress; September 19-21, 2020.
4. Davies, M., Duffield E., Durvalumab Immunotherapy: Nursing Management of Immune-Related Adverse Events During the Journey of Patients With Stage III Non-Small Cell Lung Cancer. Clin J Oncol Nurs. 2020 Jun 1;24(3):277-283.
5. Santini FC, Rizvi H, Plodkowski AJ, et al. Safety and efficacy of re-treating with immunotherapy after immune-related adverse events in patients with NSCLC.
6. Sheth S, Gao C, Mueller N*, et al*. Durvalumab activity in previously treated patients who stopped durvalumab without disease progression. *Journal for ImmunoTherapy of Cancer* 2020;8:e000650.