DURV Regimen
Durvalumab

Disease Site  | Lung - Non-Small Cell
---|---
Intent  | Curative
Regimen Category  | Evidence-Informed:

Regimen is considered appropriate as part of the standard care of patients; meaningfully improves outcomes (survival, quality of life), tolerability or costs compared to alternatives (recommended by the Disease Site Team and national consensus body e.g. pan-Canadian Oncology Drug Review, pCODR). Recommendation is based on an appropriately conducted phase III clinical trial relevant to the Canadian context OR (where phase III trials are not feasible) an appropriately sized phase II trial. Regimens where one or more drugs are not approved by Health Canada for any indication will be identified under Rationale and Use.

Rationale and Uses  | Treatment of patients with locally advanced unresectable non-small cell lung cancer (NSCLC) whose disease has not progressed following platinum-based chemoradiation therapy.
---|---

durvalumab  | 10 mg /kg IV Day 1
(This drug is not currently publicly funded for this regimen and intent)
C - Cycle Frequency

REPEAT EVERY 14 DAYS

For a usual total of up to 12 cycles unless disease progression or unacceptable toxicity occurs.

D - Premedication and Supportive Measures

Antiemetic Regimen: Minimal

Consider pre-medication in patients with prior infusion related reactions.

E - Dose Modifications

Doses should be modified according to the protocol by which the patient is being treated.

Dosage with toxicity

- Healthcare professionals should also consult the most recent durvalumab product monograph for additional information.

Summary of Principles of Management of Immune-Related Adverse Effects (irAEs)

- Immune-related adverse effects (irAEs) are different in their presentation, onset and duration compared to conventional chemotherapy. Patient and provider education is essential.

- Initial irAE presentation can occur months after completion of treatment and affect multiple organs.

- Dose escalation or reduction is not recommended.

- If no other cause can be identified (such as infection), any new symptom should be considered immune-related and prompt treatment initiated.

- Organ-specific system-based toxicity management is recommended.

- Refer to CCO's Immune Checkpoint Inhibitor Toxicity Management Guideline for detailed descriptions of Immune-related toxicities and their management.
Management of Infusion related Reactions

<table>
<thead>
<tr>
<th>Severity</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1 or 2</td>
<td>Interrupt or slow the rate of infusion by 50%. Consider pre-medications prior to subsequent infusions.</td>
</tr>
<tr>
<td>Grade 3 or 4</td>
<td>Discontinue</td>
</tr>
</tbody>
</table>

Hepatic Impairment

Refer to CCO’s Immune Checkpoint Inhibitor Toxicity Management Guideline for detailed descriptions for immune-related hepatitis management.

<table>
<thead>
<tr>
<th>Hepatic impairment</th>
<th>Durvalumab dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild (bilirubin ≤ ULN and AST &gt; ULN or bilirubin &gt;1 to ≤1.5 x ULN and any AST)</td>
<td>No dosage adjustment is required</td>
</tr>
<tr>
<td>Moderate (total bilirubin &gt; 1.5 - ≤3 x ULN and any AST) or Severe (total bilirubin &gt; 3 x ULN and any AST)</td>
<td>No data</td>
</tr>
</tbody>
</table>

Renal Impairment

Refer to CCO's Immune Checkpoint Inhibitor Toxicity Management Guideline for detailed descriptions for immune-related nephritis management.

<table>
<thead>
<tr>
<th>Renal impairment</th>
<th>Durvalumab dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild to Moderate (CrCl ≥ 30 ml/min)</td>
<td>No dosage adjustment is required</td>
</tr>
<tr>
<td>Severe (CrCl &lt; 30 ml/min)</td>
<td>No data</td>
</tr>
</tbody>
</table>

Dosage in the Elderly
No dosage adjustment is required for patients aged 65 and older.

F - Adverse Effects

Refer to durvalumab drug monograph(s) for additional details of adverse effects

<table>
<thead>
<tr>
<th>Common (25-49%)</th>
<th>Less common (10-24%)</th>
<th>Uncommon (&lt; 10%), but may be severe or life-threatening</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cough</td>
<td>Rash/pruritus (may be severe)</td>
<td>Hepatitis</td>
</tr>
<tr>
<td>Pneumonitis (including radiation pneumonitis and interstitial lung disease (may be severe)</td>
<td>Diarrhea (may be severe - colitis)</td>
<td>Creatinine increased / nephritis</td>
</tr>
<tr>
<td>Infection</td>
<td>Hypothyroidism</td>
<td>Hyperthyroidism</td>
</tr>
<tr>
<td></td>
<td>Abdominal pain</td>
<td>Infusion related reaction</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Adrenal insufficiency</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hypophysitis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Type 1 diabetes mellitus</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Immune thrombocytopenic purpura</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Myositis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Myocarditis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Uveitis</td>
</tr>
</tbody>
</table>

G - Interactions

Refer to durvalumab drug monograph(s) for additional details

No formal pharmacokinetic drug-drug interaction studies have been conducted.
H - Drug Administration and Special Precautions

Refer to durvalumab drug monograph(s) for additional details

Administration

- Administer by IV infusion over 60 minutes using a sterile, low-protein binding 0.2-0.22 micron in-line filter.
- Durvalumab is supplied as a single-use, preservative-free vial.
- Visually inspect the vial for particulates and discolouration prior to dilution. Undiluted solution should be clear to opalescent and colorless to slightly yellow.
- Using aseptic technique, withdraw the required drug volume and transfer to an IV bag of NS or D5W to a final concentration of 1 to 15 mg/ml.
- Mix by gentle inversion; do not shake.
- Do not co-administer with other drugs; flush line after each dose.
- Store unused drug vials under refrigeration (2-8°C) in the original package.
- Protect from light and do not freeze.

Contraindications

- Patients who have a hypersensitivity to this drug or any of its components.

Warnings/Precautions

- Use with caution and monitor closely in patients with pre-existing conditions such as colitis, hepatic impairment, respiratory or endocrine disorders, such as hypo or hyperthyroidism or diabetes mellitus.
- Patients with a history of immunodeficiency; medical conditions that required systemic immunosuppression; history of severe immune-mediated adverse reactions; untreated CNS metastases; HIV; active tuberculosis, or hepatitis B or C infection were excluded from trials.
Pregnancy/Lactation

- Durvalumab may cause fetal harm and is not recommended for use in pregnancy. Adequate contraception should be used by both sexes during treatment, and for at least 3 months after the last dose.

- Breastfeeding is not recommended during treatment and for at least 3 months after the last dose.
  - Immunoglobulins are known to be secreted into breast milk; therefore as a human IgG1k antibody, there is potential for infant exposure to durvalumab via breast milk.

- Fertility Effects: Unknown

I - Recommended Clinical Monitoring

Recommended Clinical Monitoring

- CBC; Baseline and before each dose
- Liver function tests; Baseline and before each dose
- Renal function tests; Baseline and before each dose
- Thyroid function tests; Baseline and before each dose or at least once per month
- Clinical toxicity assessment for infection, bleeding, infusion reactions, immune-mediated reactions, including GI, skin, ocular, respiratory, cardiac, musculoskeletal, hepatic, renal, hematologic, and endocrine toxicities; At each visit
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

J - Administrative Information

Approximate Patient Visit 1.5 hours
K - References


Durvalumab drug monograph, Cancer Care Ontario.


February 2019 Updated regimen abstract to full monograph.

M - Disclaimer

Regimen Abstracts

A Regimen Abstract is an abbreviated version of a Regimen Monograph and contains only top level information on usage, dosing, schedule, cycle length and special notes (if available). It is intended for healthcare providers and is to be used for informational purposes only. It is not intended to constitute or be a substitute for medical advice, and all uses of the Regimen Abstract are subject to clinical judgment. Such information is provided on an “as-is” basis, without any representation, warranty, or condition, whether express, or implied, statutory or otherwise, as to the information’s quality, accuracy, currency, completeness, or reliability, and Cancer Care Ontario disclaims all liability for the use of this information, and for any claims, actions, demands or suits that arise from such use.

Information in regimen abstracts is accurate to the extent of the ST-QBP regimen master listings, and has not undergone the full review process of a regimen monograph. Full regimen monographs will be published for each ST-QBP regimen as they are developed.

Regimen Monographs

Refer to the New Drug Funding Program or Ontario Public Drug Programs websites for the most up-to-date public funding information.

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