Continuing the momentum in SCLC: Exploring second-line and novel therapy options

Conversation 1

Considering the second-line treatment choices for SCLC

Dr Barbara Melosky
Medical Oncologist

Dr Sonia Amin Thomas
Oncology Pharmacist

Patient case study: Initial treatment

Presentation

62-year-old man

Smoking history:
Two packs per day for 30 years; quit 7 years ago

Past medical history:
Hypertension

Presenting symptoms:
ED visit because disorientated; not eating, 15-lb weight loss in the past 3 weeks

Findings

CT abdomen/pelvis/chest:
4.3 × 3.2 × 4.6 cm right lower lobe mass, extensive lymphadenopathy throughout the neck and chest, liver metastases

ECOG PS: 1

Lab results:

- Na: 126 mmol/L
- K: 4.6 mmol/L
- SCr: 76.04 µmol/L
- Bilirubin: 1.2 mg/dL
- WBC: 6,500/mm^3
- Platelets: 238,000/mm^3
- AST/ALT: 45/68 units/L

Treatment

Initial treatment:
Patient completed four cycles of chemoimmunotherapy (atezolizumab + carboplatin + etoposide) and was restaged with a PET/CT, which showed stable disease

Maintenance therapy:
Atezolizumab every 21 days

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CT, computerized tomography; ECOG PS, Eastern Cooperative Oncology Group Performance Status; ED, emergency department; ES-SCLC, extensive stage small cell lung cancer; PET, positron emission tomography; SCr, serum creatinine; WBC, white blood cells.

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Patient case study: Disease progression

Presentation

5 months into maintenance therapy, the patient called the clinic complaining of increasing shortness of breath

Findings

CT confirms disease recurrence

Treatment

What is the best treatment for disease recurrence in this patient?

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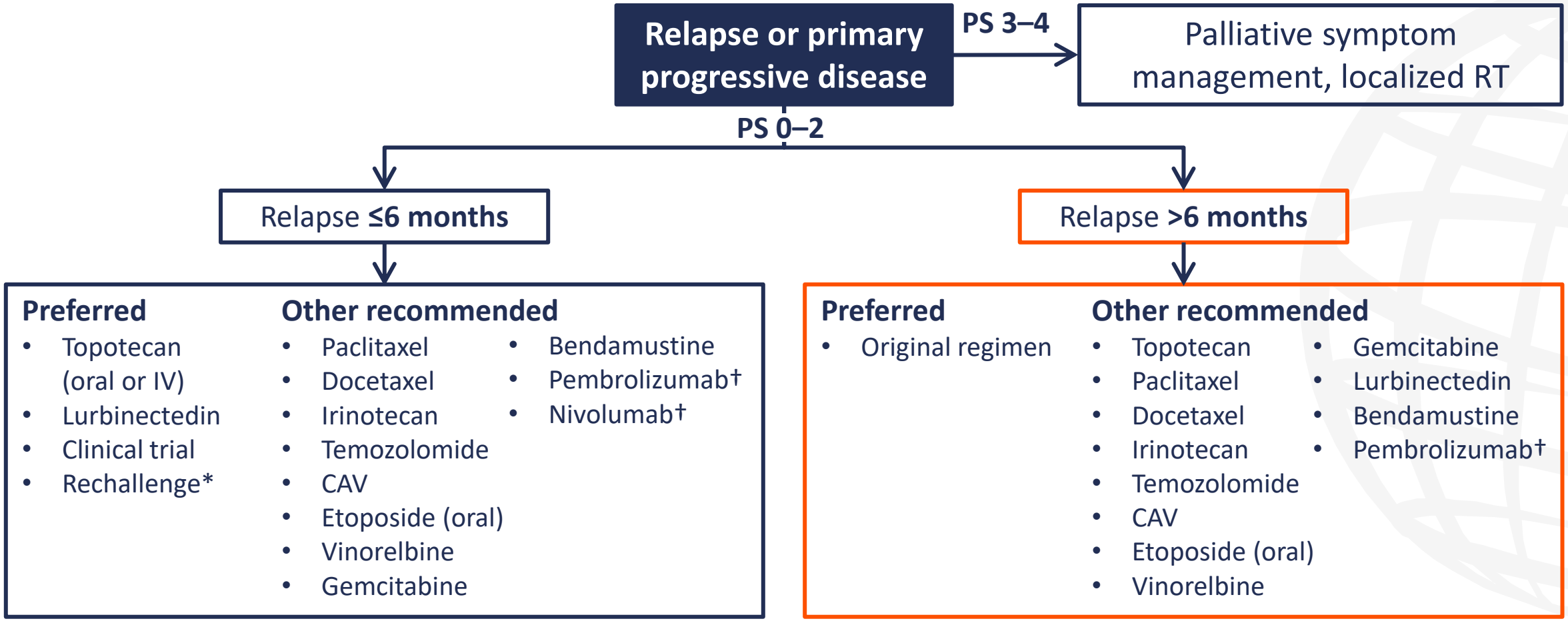
CT, computerized tomography.

Treatment algorithm post-first line



*Rechallenging with the original or similar platinum-based regimen should be considered if there has been a disease-free interval of 3–6 months.
†The FDA has withdrawn pembrolizumab and nivolumab for patients with relapsed SCLC but the agents are still recommended by the NCCN panel for certain patients.
CAV, cyclophosphamide/doxorubicin/vincristine; IV, intravenous; NCCN, National Comprehensive Cancer Network; PS, performance status; RT, radiotherapy; SCLC, small cell lung cancer.
NCCN Clinical Practice Guidelines in Oncology. Small Cell Lung Cancer. Version 1.2023. 25 August 2022. Available at: www.nccn.org/professionals/physician_gls/pdf/sclc.pdf (accessed 19 October 2022).

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Conversation 2

Tailoring treatment choices to the patient with relapsed SCLC

Dr Barbara Melosky
Medical Oncologist

Dr Christine Argento
Pulmonologist

Patient case study: Presentation

History

65-year-old man

Smoking history:
Smoked intermittently for ~40 years

Past medical history:
ES-SCLC with brain metastases

Received two cycles of atezolizumab + etoposide + carboplatin

Presentation

Presenting symptoms:
Chills for 2 weeks, cough for 7 days, onset with weakness

Initial findings:
Fever, hypoxia (80%)

Initial treatment

4 L O_2 by nasal cannula

ES-SCLC, extensive stage small cell lung cancer.

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Patient case study: Findings

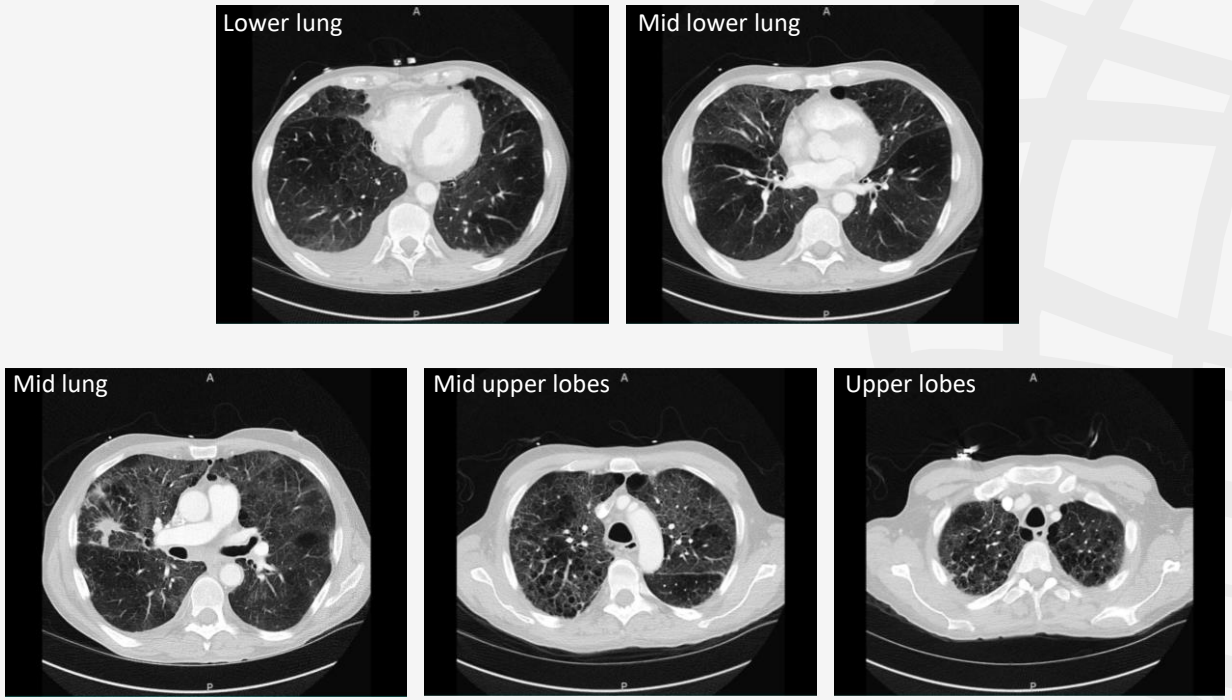
Findings

RVP and blood culture: Negative

CTA:

- No pulmonary embolism
- Spiculated RML mass with interval perilesional reticular and ground-glass opacity, and obscured borders
- Other metastatic pulmonary nodules decreased in size
- Interstitial reticulations in the RUL, RML and LUL with increased prominence in the RLL since last exam
- No metastatic spread noted in abdomen

CTA chest



CTA, computerized tomography angiography; LUL, left upper lobe; RLL, right lower lobe; RML, right middle lobe; RUL, right upper lobe; RVP, respiratory virus panel.

Patient case study: Treatment and follow-up

Treatment

Patient became tachypnoeic and hypoxic (91%)

4 L O_2 by nasal cannula
Cefepime 2 g
Vancomycin
1 L bolus LR

Fever returned, patient became hypotensive and tachycardic

HFNC at 50 L/min
1 L bolus LR, LR drip
Azithromycin added

Diagnosis

Pneumonia and suspected **checkpoint inhibitor pneumonitis**

↓

Patient completed a course of **cefepime** for **pneumonia** and **methylprednisolone 2 mg/kg** for possible **checkpoint inhibitor pneumonitis**

Typical treatment for checkpoint inhibitor pneumonitis

- Methylprednisolone 2mg/kg IV
- Plan for a 6–8 week course of steroids; decrease 10 mg per week until 20 mg/day, then decrease by 10 mg every 2 weeks
- Pneumocystis prophylaxis for prolonged high-dose steroids
- No need for additional irAE-directed therapy (e.g. IVIG)
- Close pulmonary and oncology follow-up and repeat CT chest in ~8 weeks

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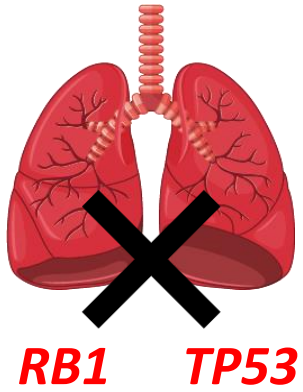
CT, computerized tomography; HFNC, high-flow nasal cannula; irAE, immune-related adverse event; IV, intravenous; IVIG, IV immune globulin; LR, lactated Ringer's.

SCLC subtypes and biomarker potential



HIGHLY EXPRESSED TRANSCRIPTION FACTORS	TRANSCRIPTIONAL SUBTYPES	POTENTIAL THERAPEUTIC APPROACH
Neuroendocrine		
ASCL1	SCLC-A	Bcl-2 inhibitors
NEUROD1	SCLC-N	AURK inhibitors
Non-neuroendocrine		
POU2F3	SCLC-P	PARP inhibitors
Immune infiltrated		
Immune genes (low expression of ASCL1, NEUROD1, POU2F3)	SCLC-I	ICI + chemotherapy (thought to be highly platinum resistant)

- SCLC subtypes based on transcription signatures are potentially promising biomarkers[1,2]
- IMpower133 gene expression analysis: Among patients in the atezolizumab arm, there was a higher proportion of LTS in the SCLC-I subgroup, but LTS were also observed in the other subgroups[2]

ASCL1, Achaete-Scute family BHLH transcription factor 1; AURK, aurora kinase; Bcl-2, B-cell lymphoma 2; ICI, immune checkpoint inhibitor; LTS, long-term survivors; NEUROD1, neurogenic differentiation 1; PARP, poly-ADP ribose polymerase; POU2F3, POU domain class 2 transcription factor 3; RB1, retinoblastoma 1; SCLC, small cell lung cancer; TP53, tumour protein p53.

1. Gay CM, et al. *Cancer Cell.* 2021;39:346–60. 2. Liu SV, et al. Presented at: ESMO 2021. 16–21 September 2021. Virtual plenary.

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Conversation 3

Optimizing outcomes through improved adverse event management

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Medical Oncologist

Dr Victoria Sherry
Oncology Nurse Practitioner

Dr Sonia Thomas
Oncology Pharmacist

Patient case study

Presentation

61-year-old man

Smoking history:
~5 pack years*; quit over 30 years ago

Past medical history:
Sustained a motor vehicle accident (hit from behind); received physical therapy but pain persisted

Findings

MRI T-L spine:
Bone lesions in the lumbar spine and pelvis

CT chest:
Right upper lobe lung mass

Bronchoscopy:
SCLC

Treatment

Initial treatment:
Palliative radiotherapy to the pelvis for pain control and atezolizumab + carboplatin + etoposide

Maintenance therapy:
Atezolizumab

*Calculated by multiplying the number of packs of cigarettes smoked per day by the number of years the person has smoked.[1]
CT, computerized tomography; MRI T-L spine, thoracic lumbar spine magnetic resonance imaging; SCLC, small cell lung cancer.

1. National Institutes of Health. National Cancer Institute. Pack year. Available at: https://www.cancer.gov/publications/dictionaries/cancer-terms/def/pack-year (accessed 7 December 2022).

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Patient case study: Disease progression

Surveillance

4 months later, surveillance CT of the chest, abdomen and pelvis showed progression in the patient's liver

Treatment

Patient was started on lurbinectedin and underwent radiofrequency ablation to his liver lesion

Follow-up

Patient returns 3 weeks after completing his first cycle of treatment with lurbinectedin complaining of **fatigue**, **nausea** and **constipation**

Blood test revealed **WBC count 2,000/mm^3**

What strategies should be employed in this patient to manage the adverse events?

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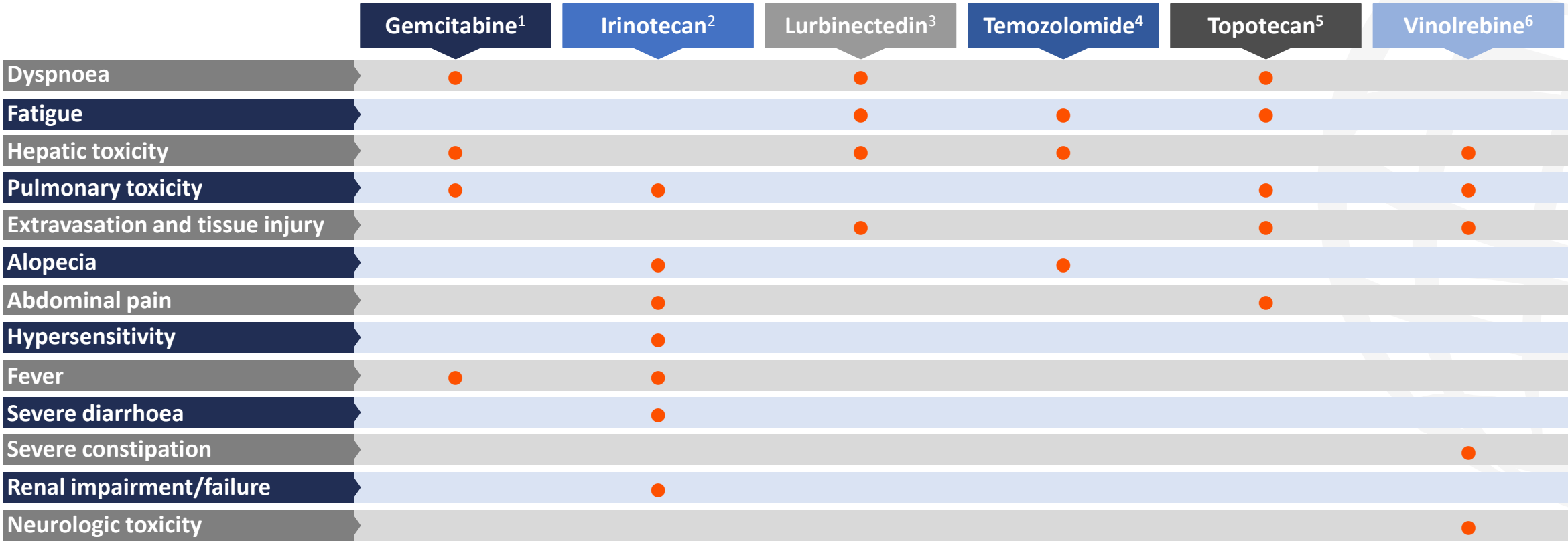
CT, computerized tomography; WBC, white blood cell.

Common side effects associated with cytotoxic treatments

Myelosuppression (anaemia, neutropenia, thrombocytopenia), **nausea/vomiting** and **embryo-foetal toxicity** are common to all agents*[1–6]



*Gemcitabine, irinotecan, lurbinectedin, temozolomide, topotecan and vinorelbine.

1. FDA. Gemcitabine US PI. Revised May 2014; 2. FDA. Irinotecan US PI. Revised January 2022; 3. FDA. Lurbinectedin US PI. Revised April 2022; 4. FDA. Temozolomide US PI. Revised November 2019; 5. FDA. Topotecan US PI. Revised June 2019; 6. FDA. Vinorelbine US PI. Revised January 2020. All available at: www.accessdata.fda.gov/scripts/cder/daf/index.cfm (accessed 28 October 2022).

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