Small Cell Lung Cancer And Competitive Landscape

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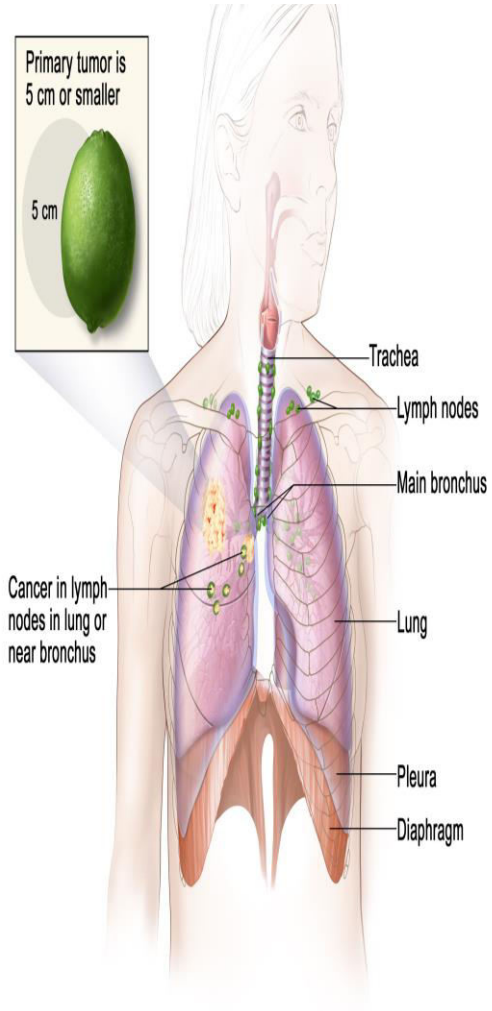
Disease Overview And Epidemiology

Disease Overview Small Cell Lung Cancer (1/2)



Description

- Squamous cell lung cancer/ Squamous cell Carcinoma is a type of lung cancer. It occurs in central part of the lung, left or right bronchus. It is a unique subset of non-small cell lung cancer. There are two types of lung cancer small cell lung cancer (SCLC) (that comprises of 10% to 15% of all lung cancers and grow and spreads faster than NSCLC) and Non small cell lung cancer (comprises of 80% to 85% of all lung cancers which is further divided into Adenocarcinoma, large cell carcinoma and squamous cell carcinoma.)

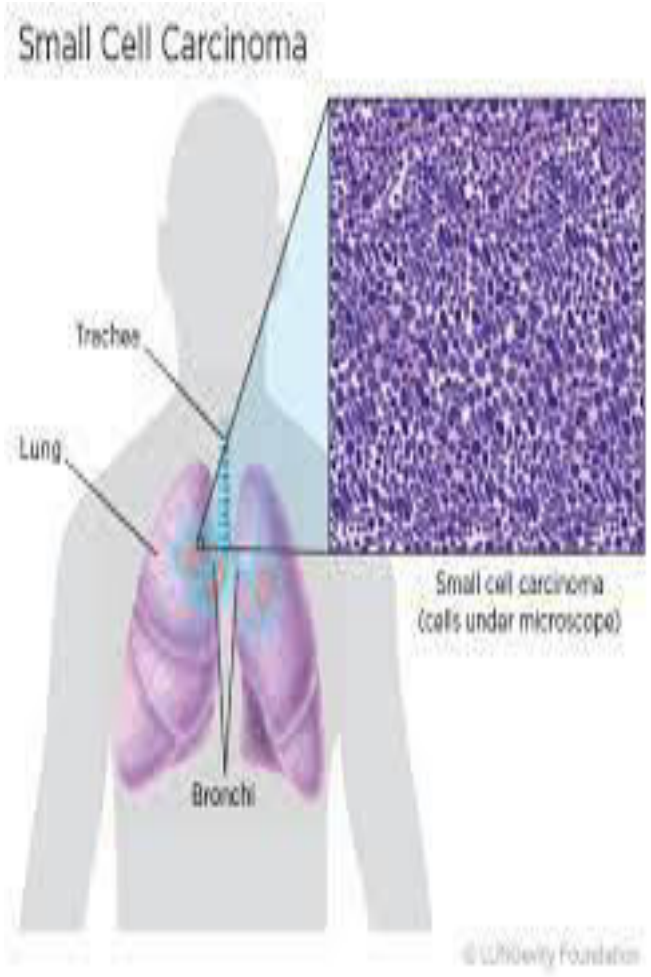
Onset/Risk Factors

- It usually starts in the cells lining bronchi and other parts of the lungs like bronchioles or alveoli.
- Risk factors include:
  - Age: Around 2 out of 3 lung cancer cases are diagnosed in people over 65 years of age.
  - Ethnicity: It is seen highest among blacks, followed by whites, American Indians/Alaska natives and Asian/Pacific Islanders.
  - Other factors: It includes Tobacco smoking, secondhand smoke, Previous radiation therapy to lungs, air pollution, personal or family history of lung cancer, and exposure to asbestos, radon and other cancer-causing agents like beryllium, arsenic, chromium compounds, mustard gas, chloromethyl ethers etc.

Symptoms and Diagnosis

- Early-stage lung cancer usually shows no signs or symptoms. It develops on the progression of the disease. This may include a cough lasting for more than 2 or 3 weeks, Chest pain, wheezing, SOB, dizziness, coughing up blood, unexplained weight loss, loss of appetite, bronchitis/pneumonia. Some fewer common symptoms may include finger clubbing, difficulty swallowing and swelling in face or neck. Advanced symptoms may include Jaundice, bone pain, face swelling, arms or neck, headache, dizziness, weak limbs and lumps in the neck and collarbone region.
- Lung cancer can be diagnosed by imaging tests like X-ray or CT scan, Sputum cytology and tissue sample

Disease Overview Small Cell Lung Cancer (2/2)



Treatments	• Various treatment options are available for lung cancer. It includes Surgery, chemotherapy, angiogenesis inhibitors, radiation therapy, targeted drug therapy and immunotherapy.
Prognosis	• The prognosis of patients affected is dependent on the stage at diagnosis. • In most of the cases survival rate is high when detected early the five-year survival rate is 99 percent.
Unmet Needs	• It is characterized by a significant level of clinical unmet need and is a disease area that has suffered from a high rate of late-stage clinical trial failure, resulting in a lack of targeted treatment options., Even though most patients experience benefit with the newer agents, many of the patients still do not have a targeted therapy. There is still a lot of scope for improvement and new treatments.
Epidemiology	• Median age of diagnosis: 65 or older • Estimated new cases in 2021: 235,760 accounting for 12.4% of all new cancer cases • Estimated deaths in 2021: 131,880 accounting for 21.7% of all cancer deaths

Competitive Landscape Overview Small Cell Lung Cancer (1/2)

4	Approved Therapies
5	Pipeline agents in Phase III development
$2.6B	Global Branded Drug Sales in 2021#
$3.4B	Forecasted Global Branded Drug Sales by 2027#
235,760	Estimated new cases of SCLC in 2021*

#Report Linker Data *Seer Data

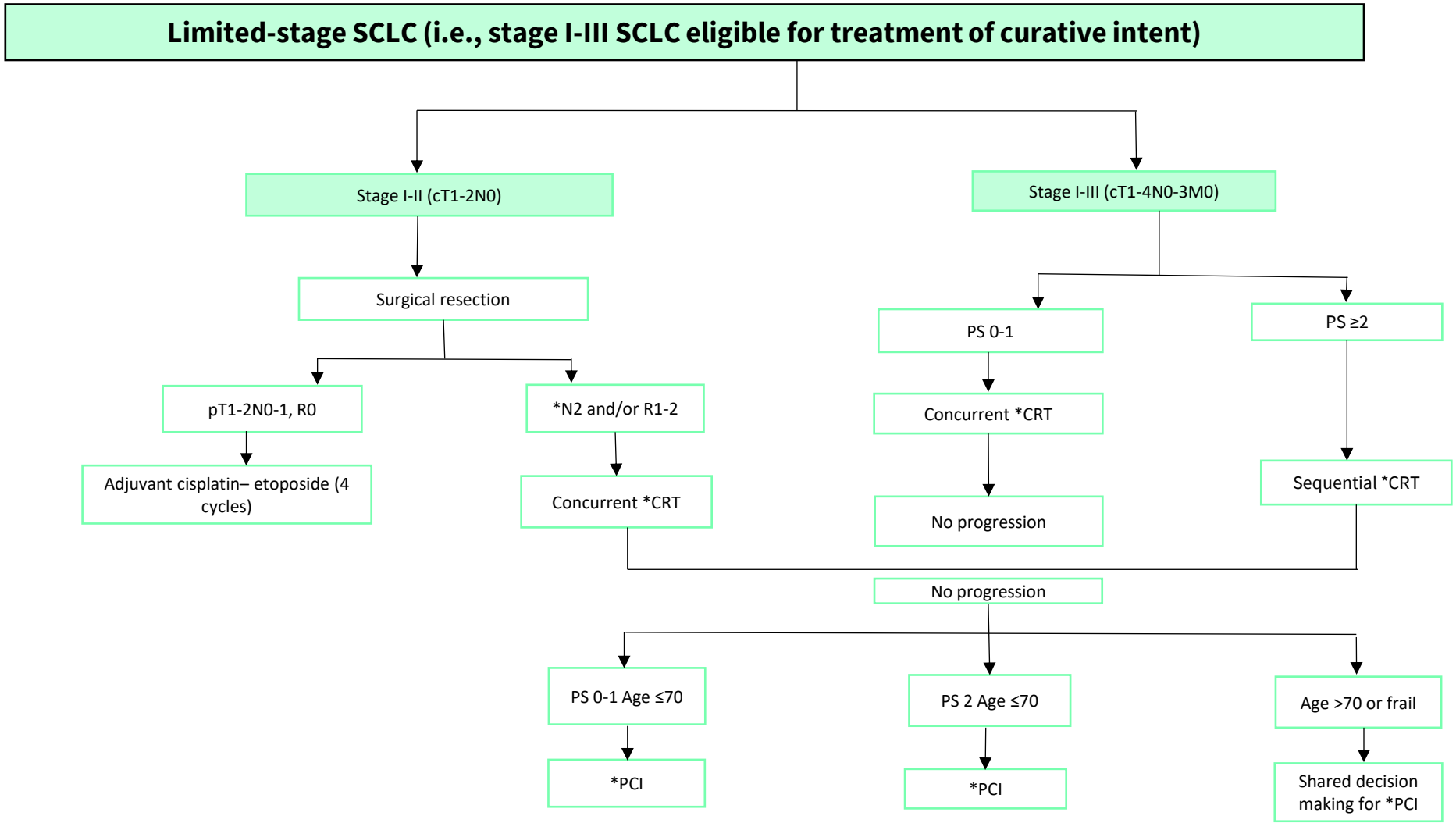
Competitive Landscape Overview Small Cell Lung Cancer (2/2)

Clinical phase	Emerging therapies**	Mechanism of Action
Phase III	Imfinzi (AstraZeneca)	PD-1 inhibitor
Phase III	Zepzelca (Jazz Pharmaceuticals)	Alkylating agent
Phase III	Keytruda (Merck)	PD-1 inhibitor
Phase II	Barasertib (AstraZeneca)	Aurora kinase B inhibitors
Phase II	Ociperlimab (BeiGene)	TIGIT protein inhibitors

**Emerging therapies are those that are in registration-seeking trials or have received Breakthrough or Fast Track designation from the FDA

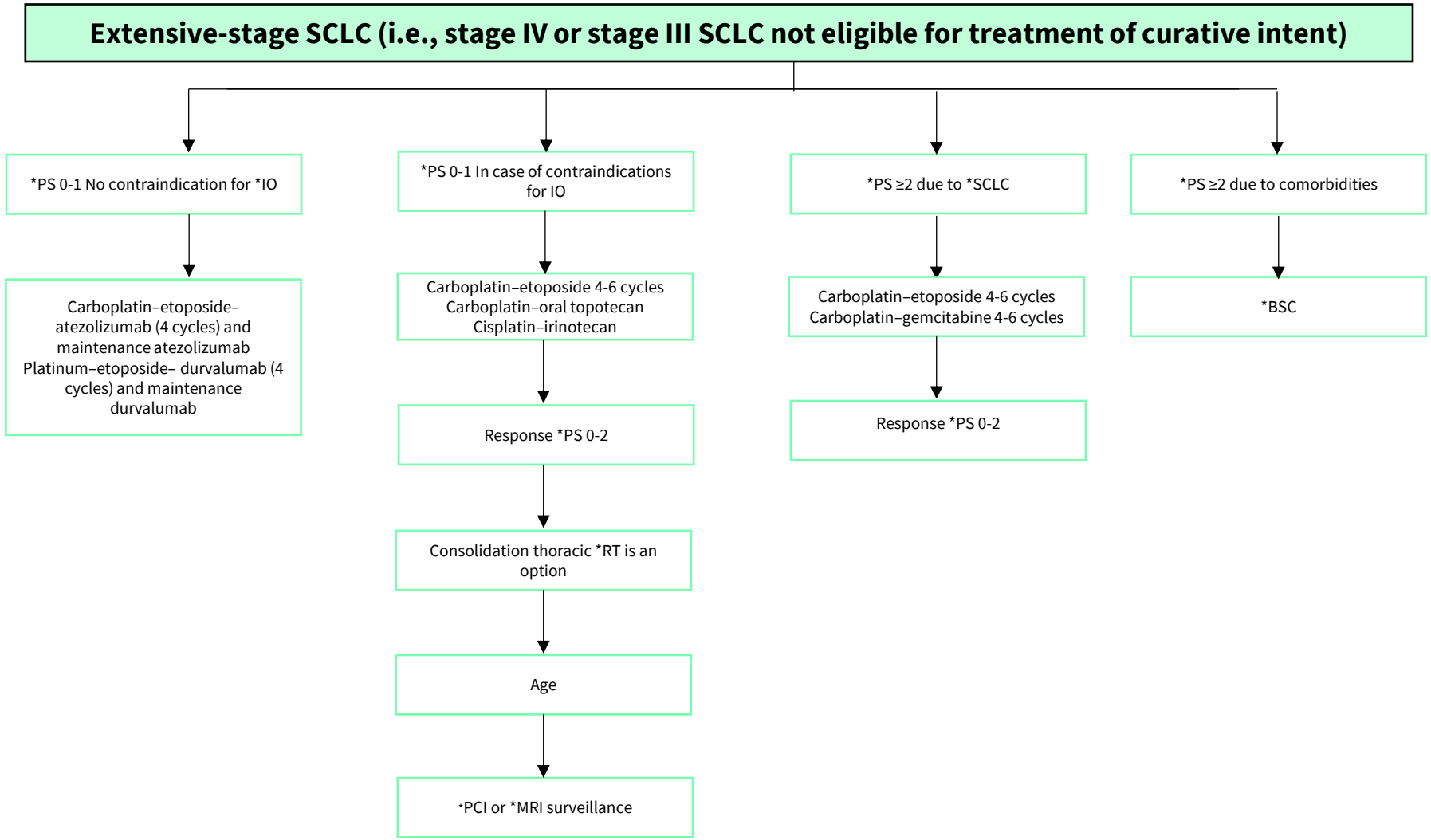
Current Treatment Algorithm

Current Treatment Algorithm Overview for SCLC (1/3)



Sources: Esmo.org; Asco; National Cancer data and International Studies Association *PCI- Prophylactic cranial irradiation *PS- performance status *N- node *R- resection *CRT- chemoradiotherapy

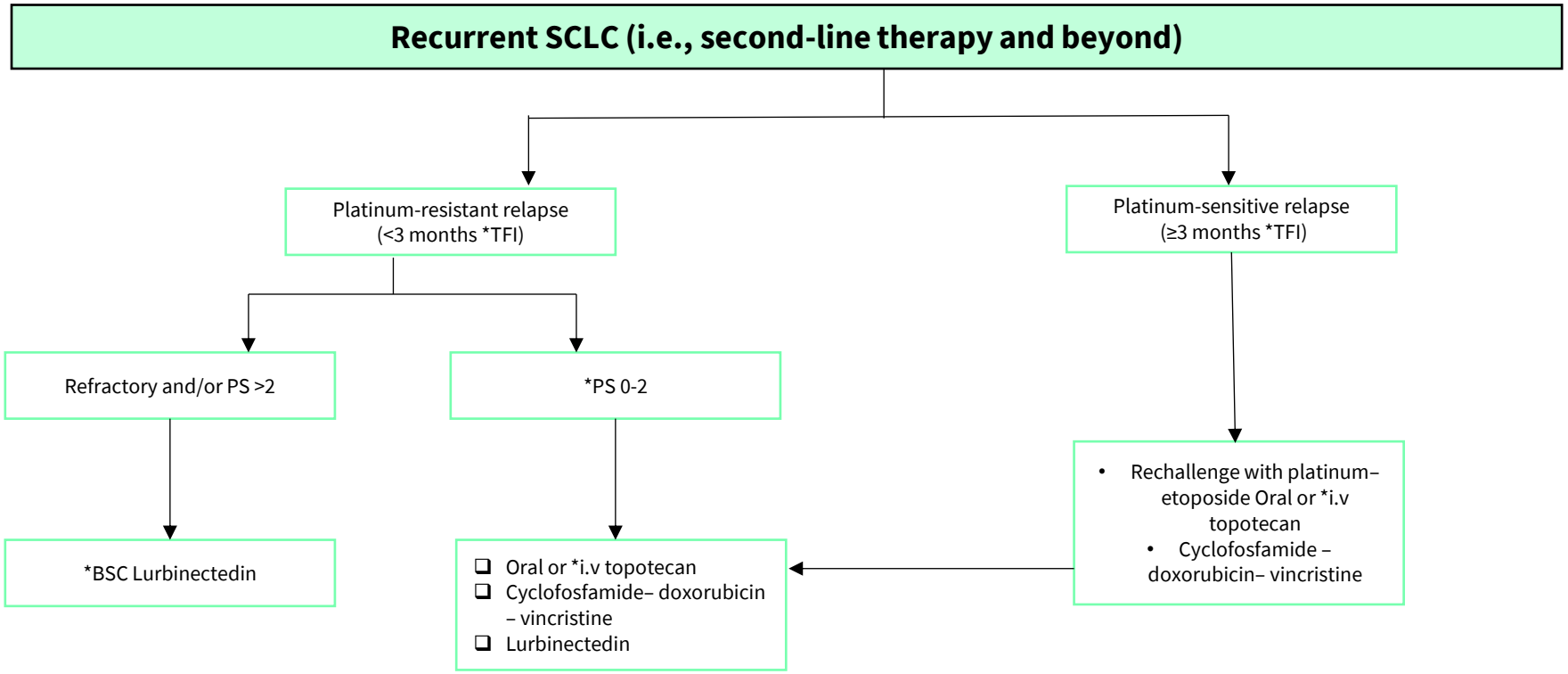
Current Treatment Algorithm Overview for SCLC (2/3)



Sources: Esmo.org; Asco, National Cancer data and International Studies Association

*SCLC- small-cell lung cancer. *BSC- Best supportive Care *PCI- prophylactic cranial irradiation *PS- performance status *IO: immunotherapy *MRI- magnetic resonance imaging *RT- radiotherapy

Current Treatment Algorithm Overview for SCLC (3/3)



Sources: Esmo.org; Asco, National Cancer data and International Studies Association

*BSC- Best supportive Care

*PS- performance status

*i.v- intravenous

*TFI- Treatment Free Interval

Treatment Paradigms – Small Cell Lung Cancer

Most Commonly Used Regimens (MAT Ending September 2021)

Line of treatment	US	EU4+UK	JP
First Line	• **(Tecentriq)** Atezolizumab/ Carboplatin/ Etoposide (41%) • Carboplatin/ Etoposide (21%) • Cisplatin/ Etoposide (11%)	• **(Tecentriq)** Atezolizumab/ Carboplatin/ Etoposide (33%) • Carboplatin/ Etoposide (23%) • Cisplatin/ Etoposide (15%)	• Carboplatin/ Etoposide (41%) • **(Tecentriq)** Atezolizumab/ Carboplatin/ Etoposide (25%) • Cisplatin/ Etoposide (14%)
Second Line	• **(Tecentriq)** Atezolizumab (25%) • Lurbinectedin (17%) • **(Imfinzi)** Durvalumab (12%)	• Topotecan (53%) • **(Tecentriq)** Atezolizumab (10%) • Cyclophosphamide/ Doxorubicin/ Vincristine (7%)	• Amrubicin (hydrochloride) (43%) • **(Tecentriq)** Atezolizumab (22%) • **(Tecentriq)** Atezolizumab/ Carboplatin/ Etoposide (7%)
Third Line	• **(Opdivo)** Nivolumab (30%) • **(Tecentriq)** Atezolizumab/ Carboplatin/ Etoposide (26%) • Lurbinectedin (21%)	• Topotecan (22%) • Vinorelbine (19%) • Cyclophosphamide/ Doxorubicin/ Vincristine (18%)	• Amrubicin (hydrochloride) (35%) • Irinotecan (22%) • Carboplatin/ Etoposide (11%)

- The treatment paradigms between US, EU5 and Japan for Metastatic SCLC are similar among 1L and 2L
  - In 1L patients in US, EU5, and JP, Atezolizumab/ Carboplatin/ Etoposide, Carboplatin/ Etoposide and Cisplatin/ Etoposide are the top 3 regimens.
  - In 2L patients in US, EU5, and JP, Atezolizumab is among the top 3 regimens
  - In 3L patients, the top regimen for US is Nivolumab (30%), the top regimen for EU5 is Topotecan (22%), and the top regimen for JP is Amrubicin (hydrochloride) (35%).

Research Question and Aim

- **Key Research Question:**

- What are the potential upcoming therapies for Small-cell Lung Cancer?
- What is the competitive timeline for current and emerging therapies in Small Cell Lung Cancer?

- **Aim:**

- The primary goal of this study is to gain a thorough understanding of the overview, current treatment algorithm, emerging treatment plans, and competitive timeline of small cell lung cancer
- The secondary goal is to comprehend the treatment landscape and competitive analysis, as well as to investigate the current SCLC treatment algorithm

Methodology (1/2)

DATA COLLECTION: Secondary Data for the study was collected from clinicaltrials.gov for Small Cell Lung Cancer

No. of trials: 254 trials of SCLC

STUDY RESEARCH CRITERIA:

- **Inclusion criteria:**
  - Trials from Phase II, Phase III and completed were included.
  - Only industry-sponsored trials were considered (US, EU, and Japan)
  - Advance filter was applied, not yet recruiting, recruiting, enrolling by invitation, active not recruiting and completed and unknown status trials were selected
  - Only industry sponsored trials were considered

Exclusion criteria:

- Preclinical, Phase I/II, Phase I, Phase IV were excluded
- Studies that were suspended, discontinued, terminated, or whose status was unknown were excluded educational institutes, research centres, hospitals, and privately funded studies were not included

Methodology (2/2)

- Assets included as **'Emerging Therapies'** fulfil the following criteria:
  - Therapies that are not previously approved as any line of therapy for the disease AND
  - Therapies that have an active Phase 2 or Phase 3 trial that is registration-directed OR
  - Therapies that have an FDA breakthrough or fast-track designation

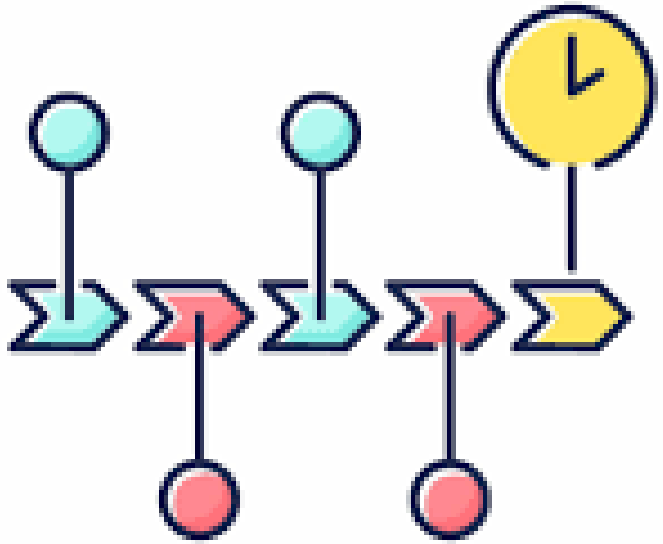
- Assets included as **'Competitors'** fulfil the following criteria:
  - Therapies that are previously approved as any line of therapy for the disease
  - Only Competitors with ongoing registrational trials in the disease are included in the section "Competitor & Emerging Therapy Timelines"
- Assets under **'Other Pipeline Therapies'** fulfil the following criteria:
  - Therapies that are not previously approved in any indication (i.e., "new molecular entity" or "new therapeutic biological products") AND
  - Therapies at P2 or higher in development but are not known to be registration-seeking

- **DATA Analysis:**

  An excel workbook was prepared in which two different sheets were made one for phase 2 and another phase 3. Relevant data was extracted on the basis of different criteria such as brand name, company name, phase, pipeline, special drug designation and results, etc. The relevant information was used to summarise heat map, current and emerging therapies and their timeline, potential upcoming therapy, emerging treatment algorithm and finally the current clinical benchmark.

Result

Competitive Heat Map and Timeline



Competitive Heat Map for Current & Emerging Therapies in SCLC

Marketed, registration-seeking, or FDA Breakthrough / Fast Track designation therapies (1/2)

Agent	ROA and MOA	1st Line	2nd Line	3rd Line and beyond
1. Tecentriq (Atezolizumab) Genentech	IV PD-1 inhibitor	**MARKETED IN US, EU, JP** IMpower133 (+ Carboplatin + Etoposide, ▲ +)		
2. Imfinzi (Durvalumab) AZ	Oral PD-1 inhibitor	**MARKETED IN US, EU, JP** CASPIAN (± tremelimumab + platinum-based chemotherapy, ▲ +) ADRIATIC (+ Tremelimumab, ▲) LUMINANCE (+ platinum chemo + etoposide)		
3. Cosela (Trilaciclib) Genentech	Oral Cyclin dependent kinase inhibitor	**MARKETED IN US, EU, JP** NCT02499770 (+ Etoposide + Carboplatin, ▲ +) NCT03041311 (+ Carboplatin + etoposide + atezolizumab, ▲ +)	**MARKETED IN US, EU, JP** NCT02514447 (SA, ▲ +)	
4. Zepzelca (Lurbinectidin) Jazz Pharmaceuticals	IV Alkylating agents	IMforte (+ Atezolizumab, ▲)	MARKETED IN US NCT02454972 (SA, ▲ +) LAGOON (SA/ + Irinotecan, ▲)	

▲ randomized SA single agent + met 1º endpoint ⦸ did not meet 1º endpoint

APPROVED | Phase III | Phase II

Competitive Heat Map for Current & Emerging Therapies in SCLC

Marketed, registration-seeking, or FDA Breakthrough / Fast Track designation therapies (2/2)

Agent	ROA and MOA	1st Line			2nd Line	3rd line and Beyond
5. Keytruda (Pembrolizumab) Merck	IV PD-1 inhibitor	KEYLYNK-013 (+ Olaparib, ▲)	REACTION (+ Chemo, ▲, +)	KEYNOTE-604 (+ Etoposide, ▲ +)		
6. Opdivo (Nivolumab) BMS	IV PD-1 inhibitor				CheckMate331 (SA, ▲, ⊘) CheckMate 451 (+ Ipilimumab, ▲, ⊘)	
7. Barasertib AZ	IV Aurora kinase B inhibitors	TAZMAN (+ Durvalumab)				
8. Ociperlimab BeiGene	IV TIGIT protein inhibitors	Phase II (+ Tislelizumab + Chemo, ▲)				

▲ randomized SA single agent + met 1º endpoint ⊘ did not meet 1º endpoint

APPROVED Phase III Phase II

Competitive Timeline for Current & Emerging Therapies in SCLC

Registration-seeking, or FDA Breakthrough / Fast Track designation therapies (1/2)

		2020				2021				2022				2023				2024				2025				2026				2027+			
First Line SCLC		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
1. Imfinzi (Durvalumab) AZ	Phase III : (+ Tremelimumab) ADRIATIC														◆																		
	Phase III : (+ platinum chemo + etoposide) LUMINANCE																						◆										
2. Zepzelca (Lurbinectidin) Jazz Pharmaceuticals	Phase III : (+ Atezolizumab) IMforte													◆																			
3. Defobarasertib AZ	Phase II : (+ Durvalumab) TAZMAN																	◆					◆										

◆ Topline Results/ Primary Completion Date US EU Japan FTD – Fast Track Designation BTD- Break through therapy

Competitive Timeline for Current & Emerging Therapies in SCLC

Registration-seeking, or FDA Breakthrough / Fast Track designation therapies (2/2)

		2020				2021				2022				2023				2024				2025				2026				2027+			
Second Line SCLC		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
1. Zepzelca (Lurbinectidin) Jazz Pharmaceuticals	Phase III : (SA) LAGOON																						◆					🇺🇸						

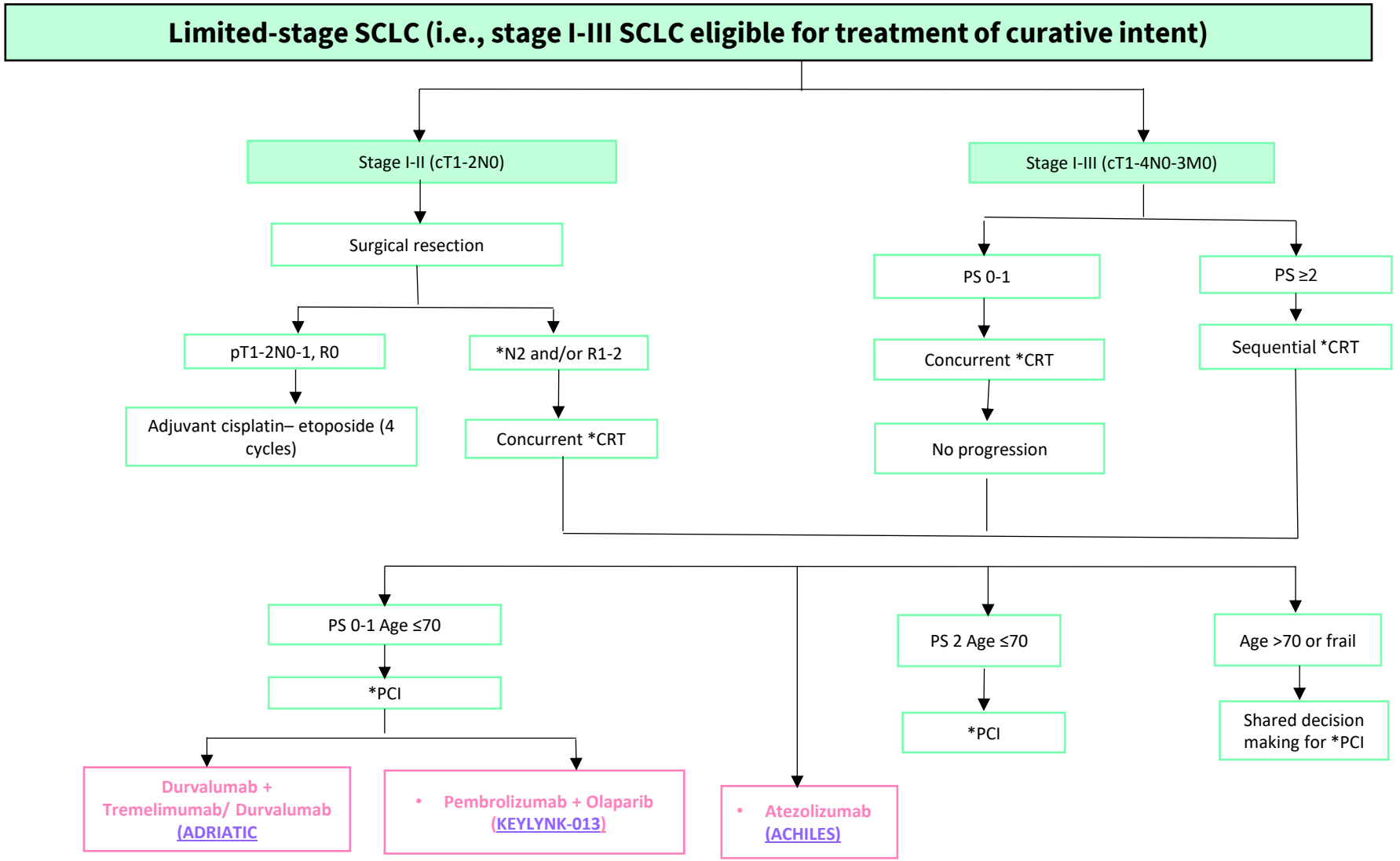
◆ Topline Results/ Primary Completion Date 🇺🇸 US EU 🇯🇵 Japan **FTD** – Fast Track Designation BTD- Break through therapy

Other Potential Upcoming Therapies

Product	Interventional Arms	Company	Disease Area	LoT	Developmental Phase	MoA	Trial ID
Pembrolizumab/Vibostolimab	**Experimental:** Pembrolizumab/Vibostolimab; **Active Comparator:** Atezolizumab	Merck Sharp & Dohme Corp.	Extensive-Stage Small Cell Lung Cancer	1L	Phase 3	PD-1 inhibitor	**KEYVIBE-008** NCT05224141
RRx-001	**Experimental:** RRx-001 + eLOOP Device; **Active Comparator:** Cisplatin/carboplatin plus etoposide;	EpicentRx, Inc.	Small Cell Lung Cancer	3L/ 3L+	Phase 3	anti-CD47-SIRPα	**(REPLATINUM)** NCT03699956
Tarlatamab	**Experimental:** Part 1: Tarlatamab Low Dose; **Experimental:** Part 1: Tarlatamab High Dose; **Experimental:** Part 2: Dose Expansion	Amgen	Relapsed/Refractory Small Cell Lung Cancer	2L/ 2L+	Phase 2	DLL3-targeting HLE BiTE® immune therapy	**(DeLLphi-301)** NCT05060016
BMS-986012	**Experimental:** Arm A: Carboplatin + Etoposide + Nivolumab + BMS-986012; **Experimental:** Arm B: Carboplatin + Etoposide + Nivolumab	Bristol-Myers Squibb	Extensive-stage Small Cell Lung Cancer	1L	Phase 2	Fucosyl GM1 ganglioside inhibitors	NCT04702880

Emerging Treatment Algorithms

Emerging Treatment Algorithm Overview for SCLC (1/3)



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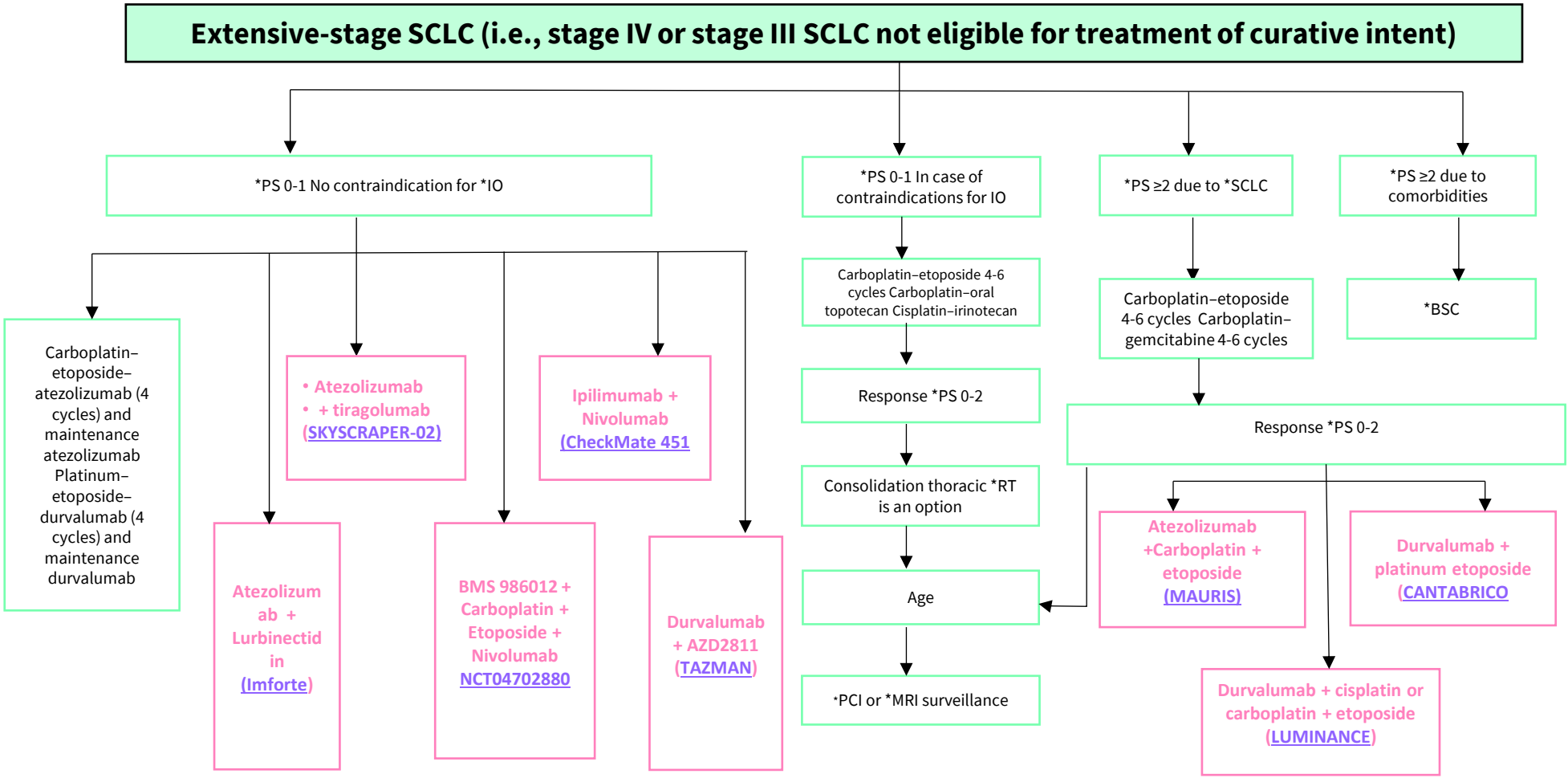
Emerging Treatment Algorithm Overview for SCLC (2/3)



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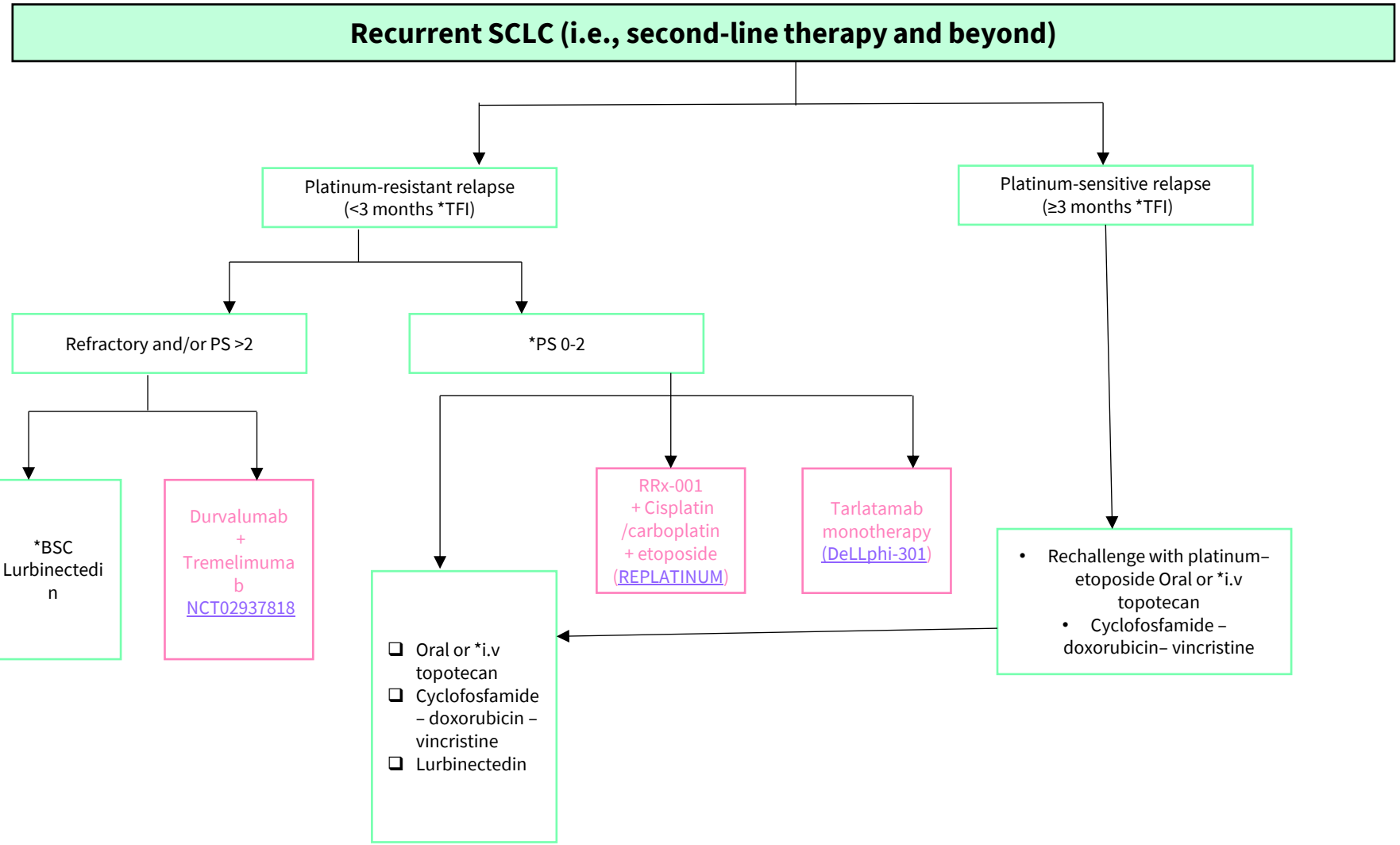
Emerging Treatment Algorithm Overview for SCLC (3/3)



Sources: Esmo.org; Asco, National Cancer data and International Studies Association

*BSC- Best supportive Care

*PS- performance status

*i.v- intravenous

*TFI- Treatment Free Interval

Current Clinical Benchmarks

Marketed Products – Small Cell Lung Cancer

First Line SCLC	Trial Description	Efficacy		Safety
TECENTRIQ **(Atezolizumab)** PD-1 inhibitor Patients With Untreated Extensive-Stage Small Cell Lung Cancer	IMpower133 (N= 403)	**Tecentriq (n = 201)** Median OS= 12.3 months Median PFS=5.2 months Median DOR= 4.2 months	**Comparator arm (n=202)** Median OS= 10.3months Median PFS=4.3 months Median DOR= 3.9 months	Fatal adverse reactions occurred in 2% of patients receiving TECENTRIQ. These included pneumonia, respiratory failure, neutropenia, and death
IMFINZI® **(durvalumab)** PD-1 inhibitor Patients With Extensive Disease Small-Cell Lung Cancer	CASPIAN (N= 978)	**Imfinzi (n=268)** Median PFS = 5.1 months Median OS= 10·4 months ORR = 68%	**Placebo (n=269)** Median PFS= 5.4 months Median OS = 10·5 months ORR = 58%	Any-cause serious adverse events were reported in the durvalumab plus tremelimumab plus platinum-etoposide group, 85 (32%) in the durvalumab plus platinum-etoposide group, and 97 (36%) in the platinum-etoposide group
COSELA **(Trilaciclib)** Cyclin-dependent kinase 4 and 6 inhibitors Untreated Extensive Stage Small Cell Lung	NCT03041311 (N=107)	**Cosela (n=54)** No of patients with neutropenia: 1 No of patients with RBC transfusion after 5 weeks: 7	**Placebo** (n=53) No of patients with neutropenia: 26 No of patients with RBC transfusion after 5 weeks: 11	Nineteen percent of patients receiving COSELA had Grade 3 or 4 decreased hemoglobin compared with 28% of patients receiving placebo
	NCT02499770 (N=77)	**Cosela (n=39)** Number of patients with severe neutropenia=2	**Placebo (n=38)** Number of patients with severe neutropenia=16	Ten percent of patients receiving COSELA had Grade 3 or 4 decreased hemoglobin compared with 18% of patients receiving placebo

Second Line SCLC	Trial Description	Efficacy			Safety
Zepzelca **(Lurbinectidin)** Alkylating agents Patients With Selected Advanced Solid Tumors	NCT02454972 (N=345)	**Zepzelca (n=105)** ORR: 35% mDOR: 5.3 months	**Zepzelca CTFI < 90 days (n=45)** ORR: 22% mDOR: 4.7 months	**Zepzelca CTFI > 90 days (n=60)** ORR: 45% mDOR: 6.2 months	Permanent discontinuation due to an adverse reaction occurred in 1.9% of patients with SCLC. Most adverse reactions were Grade 1 or 2
COSELA **(Trilaciclib)** Cyclin-dependent kinase 4 and 6 inhibitors **Untreated Extensive Stage Small Cell Lung**	NCT02514447 (N=61)	**Cosela (n=32)** DSN (days): mean (SD)= 2 (3.9) Number (%) of patients with severe neutropenia= 13 (40.6%)		**Placebo (n=29)** DSN (days): mean (SD)= 7 (6.2) Number (%) of patients with severe neutropenia= 22 (75.9%)	Thirty-eight percent of patients receiving COSELA had Grade 3 or 4 decreased hemoglobin compared with 59% of patients receiving placebo

Disscusion

Disscusion

- The preliminary understanding of the undertaken research suggested that the treatment of small cell lung cancer (SCLC) is characterized by a significant level of clinical unmet need and is a disease area that has suffered from a high rate of late-stage clinical trial failure, resulting in a lack of targeted treatment option which is, to some extent, based on the limited underlying understanding of SCLC biology.
- The open-source data available aided in the identification of the epidemiology of the disease to understand the extent and probability of wide-spreading, risk factors, available treatments, and unmet needs. Hence, it directed the research toward the two major goals - the identification of potential upcoming therapies and the competitive timeline.

Conclusion

Conclusion

- The potential upcoming therapies treatment paradigm was promising and included a multitude of molecules that are currently under later development phases.
- It was evident that the current R&D efforts are not limited to a single stage of disease and were rather distributed in early as well as later stages
- The most optimistic treatment and combinations were durvalumab + tremelimumab, pembrolizumab + olaparib, and atezolizumab in stage I-III SCLC. In the extensive-stage SCLC, atezolizumab, durvalumab, and ipilumab combinations with the standard of care chemotherapy were evident. Lastly, in the recurrent SCLC, durvalumab + tremelimumab, RRs-001 + SoC, and tarlatamb monotherapy were the major ones.

Recommendation

Recommedation

- The research can support potential players in the market to identify the most suitable time for planning their launch in order to have minimum competitors and maximum market share


Thank
you