

American Radium Society (ARS) Appropriate Use Criteria:

Accelerated Hypofractionated Radiotherapy for Locally-Advanced Non-Small Cell Lung Cancer



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BACKGROUND:

- Accelerated hypofractionated (hypofx) radiation (RT) is increasingly used for locally-advanced (LA) non-small cell lung cancer (NSCLC) ineligible for concurrent chemotherapy
- There is little randomized evidence guiding accelerated hypofractionation for LA-NSCLC
- The ARS Thoracic Appropriate Use Criteria (AUC) Panel evaluated accelerated hypofx RT in context of multidisciplinary management of LA-NSCLC

METHODOLOGY:

- 15 member ARS Thoracic AUC Panel
- 5 clinical variants of LA-NSCLC developed
- English medical literature reviewed 2010-2025 for prospective clinical trials for concurrent chemotherapy ineligible LA-NSCLC
- Modified-Delphi consensus with respect to appropriateness of RT technique, RT fractionation, and PD-L1 immunotherapy.
- Recommendations approved by ARS Executive Committee and subject to public comment

LITERATURE SEARCH RESULTS:

- Total articles, N = 228
- Prospective studies, N = 14
 - Registries, N = 4
 - Phase 1-2, N = 9
 - Phase 3, N = 1

Variant 1: An 80-year-old patient with AJCC 8th Edition, Stage IIB, cT2aN1M0 right upper lobe non-small cell lung adenocarcinoma that is PD-L1 20% who is medically unfit for surgery or concurrent chemotherapy. **A, appropriate; M, may be appropriate; U, inappropriate.**



Treatment	Rating Category	Final Tabulations								Group Median Rating
		1	2	3	4	5	6	7	8	
3D-conformal radiotherapy	M	0	0	1	3	4	1	0	0	0
Intensity-modulated radiation therapy	A	0	0	0	0	0	0	4	2	5
Proton therapy	A	0	0	0	0	0	2	5	2	0
45 Gy in 15 fractions	U	2	2	4	0	0	0	0	0	3
50-55.5 Gy in 15 fractions	M	0	0	0	1	7	1	0	0	5
60 Gy in 15 fractions	A	0	0	0	1	0	1	5	5	0
55-60 Gy in 20 fractions	A	0	0	0	0	2	0	6	3	1
60 Gy in 30 fractions	A	0	0	0	0	0	0	4	4	1
Induction PD-1/PD-L1 immunotherapy	U	1	3	4	1	0	0	0	0	3
Concurrent PD-1/PD-L1 immunotherapy	U	2	4	6	0	0	0	0	0	3
Consolidative PD-1/PD-L1 immunotherapy	A	0	0	0	0	0	0	5	4	0

Variant 2: An 80-year-old patient with AJCC 8th Edition, Stage IIB, cT4N0M0 left upper lobe non-small cell lung adenocarcinoma **abutting the heart** that is PD-L1 20% who is medically unfit for surgery or concurrent chemotherapy.



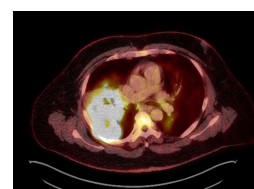
Treatment	Rating Category	Final Tabulations								Group Median Rating
		1	2	3	4	5	6	7	8	
3D-conformal radiotherapy	U	3	2	3	1	0	1	0	0	2
Intensity-modulated radiation therapy	A	0	0	0	0	0	0	6	3	8
Proton therapy	A	0	0	0	1	0	1	4	4	2
45 Gy in 15 fractions	M	0	0	0	2	5	2	0	0	5
50-55.5 Gy in 15 fractions	M	0	0	0	0	4	4	1	0	6
60 Gy in 15 fractions	N/A	0	0	0	2	2	2	2	1	6
55-60 Gy in 20 fractions	A	0	0	0	0	0	2	9	1	0
60 Gy in 30 fractions	A	0	0	0	0	0	0	3	4	2
Induction PD-1/PD-L1 immunotherapy	U	1	4	4	0	0	0	0	0	2
Concurrent PD-1/PD-L1 immunotherapy	U	3	4	5	0	0	0	0	0	2
Consolidative PD-1/PD-L1 immunotherapy	A	0	0	0	0	0	0	4	5	0

Variant 3: An 80-year-old patient with AJCC 8th Edition, Stage IIIA, cT2aN2M0 right upper lobe non-small cell lung adenocarcinoma with mediastinal station 7 **abutting the esophagus** that is PD-L1 20% who is medically unfit for surgery or concurrent chemotherapy.



Treatment	Rating Category	Final Tabulations								Group Median Rating
		1	2	3	4	5	6	7	8	
3D-conformal radiotherapy	U	3	2	5	0	2	0	0	0	3
Intensity-modulated radiation therapy	A	0	0	0	0	0	5	4	3	8
Proton therapy	A	0	0	0	1	0	2	7	2	0
45 Gy in 15 fractions	U	0	3	4	1	1	0	0	0	3
50-55.5 Gy in 15 fractions	M	0	0	0	1	5	3	0	0	5
60 Gy in 15 fractions	U	0	3	4	0	1	1	0	0	3
55-60 Gy in 20 fractions	A	0	0	0	0	2	1	8	1	0
60 Gy in 30 fractions	A	1	0	0	1	0	1	8	1	0
Induction PD-1/PD-L1 immunotherapy	U	3	3	2	1	0	0	0	0	2
Concurrent PD-1/PD-L1 immunotherapy	U	4	4	4	0	0	0	0	0	2
Consolidative PD-1/PD-L1 immunotherapy	A	0	0	0	0	0	0	5	4	0

Variant 4: An 80-year-old patient with AJCC 8th Edition, Stage IIIC, cT4N3M0 right lower lobe bulky non-small cell lung adenocarcinoma with bilateral mediastinal nodal disease that is PD-L1 20% who is medically unfit for surgery or concurrent chemotherapy.



Treatment	Rating Category	Final Tabulations								Group Median Rating
		1	2	3	4	5	6	7	8	
3D-conformal radiotherapy	U	4	2	5	0	0	0	1	0	3
Intensity-modulated radiation therapy	A	0	0	0	0	0	0	3	5	4
Proton therapy	A	0	0	2	0	0	0	5	3	2
45 Gy in 15 fractions	M	0	0	0	4	4	1	0	0	5
50-55.5 Gy in 15 fractions	M	0	0	0	2	4	2	1	0	5
60 Gy in 15 fractions	U	0	2	6	0	0	0	1	0	3
55-60 Gy in 20 fractions	A	0	0	0	0	0	1	3	4	1
60 Gy in 30 fractions	A	0	0	0	0	2	0	9	1	0
Induction PD-1/PD-L1 immunotherapy	M	1	0	0	2	4	2	0	0	5
Concurrent PD-1/PD-L1 immunotherapy	U	4	3	5	0	0	0	0	0	2
Consolidative PD-1/PD-L1 immunotherapy	A	0	0	0	0	0	0	3	5	1

Variant 5: n 80-year-old patient with AJCC 8th Edition, Stage IIIB, cT2bN3M0 right upper lobe non-small cell lung adenocarcinoma **with supraclavicular nodal disease** that is PD-L1 20% who is medically unfit for surgery or concurrent chemotherapy.

Treatment	Rating Category	Final Tabulations								Group Median Rating
		1	2	3	4	5	6	7	8	
3D-conformal radiotherapy	U	4	1	5	1	0	1	0	0	3
Intensity-modulated radiation therapy	A	0	0	0	0	0	0	4	5	3
Proton therapy	A	0	0	1	0	0	2	5	4	0
45 Gy in 15 fractions	M	0	0	0	4	3	2	0	0	5
50-55.5 Gy in 15 fractions	M	0	0	0	1	5	2	1	0	5
60 Gy in 15 fractions	U	0	0	0	0	0	0	1	0	3
55-60 Gy in 20 fractions	A	0	0	0	0	0	0	1	4	3
60 Gy in 30 fractions	A	0	0	0	0	0	1	1	8	2
Induction PD-1/PD-L1 immunotherapy	M	1	0	0	2	5	1	0	0	5
Concurrent PD-1/PD-L1 immunotherapy	U	3	3	6	0	0	0	0	0	3
Consolidative PD-1/PD-L1 immunotherapy	A	0	0	0	0	0	0	2	6	1

SUMMARY OF RECOMMENDATIONS:

- Utilize IMRT and proton therapy with accelerated hypofractionation
- Accelerated Hypofx Constraints:
 - Lung V20Gy<30%
 - Heart V40Gy<20%
 - Esophagus <55 Gy
 - Brachial plexus <50 Gy
- Doses of 60-70 Gy in 30-35 fractions or 55-60 Gy in 20 fractions usually appropriate
- Dose 45-60 Gy in 15 may be appropriate in specific clinical circumstances
- Induction immunotherapy inappropriate except bulky/N3
- Concurrent PD-L1 immune therapy with RT therapy inappropriate
- Consolidative PD-L1 immune therapy after RT to be considered
- Shared decision making is key