LINEE GUIDA 2023 PER IL TRATTAMENTO DEL TUMORE POLMONARE NON A PICCOLE CELLULE (NSCLC)

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TRATTAMENTO DEL NSCLC IN STADIO PRECOCE E LOCALMENTE AVANZATO NEL PAZIENTE ANZIANO E CON PS ≥ 2 E LOCALMENTE AVANZATO

TRATTAMENTO DEL NSCLC IN STADIO PRECOCE E LOCALMENTE AVANZATO NEL PAZIENTE ANZIANO E CON PS ≥ 2

Sono stati riportati i dati relativi ai 155 pazienti con età ≥ 65 anni arruolati nello studio JBR.10 che randomizzava i pazienti allo stadio IB-II radicalmente operati a ricevere cisplatino + vinorelbina o controllo [156]. Le caratteristiche dei pazienti erano ben bilanciate ad eccezione dell'istologia (adenocarcinoma: 58% nei giovani, 43% negli anziani; squamoso: 32% nei giovani, 49% negli anziani; p = 0.001) e il PS (PS 0: 53% nei giovani, 41% negli anziani; p = 0.01). La chemioterapia adiuvante ha significativamente migliorato la sopravvivenza degli anziani con un HR di 0.61 (p = 0.04), beneficio simile a quello riportato nella popolazione generale. L'intensità di dose mediana è stata significativamente inferiore negli anziani rispetto ai giovani con il cisplatino 14.1 mg/m²/settimana versus 18 mg/m²/settimana (p = 0.001) e la vinorelbina 9.9 mg/m²/settimana versus 13.2 mg/m²/settimana (p = 0.004), rispettivamente. Pertanto, gli anziani hanno ricevuto una intensità di dose più bassa di vinorelbina (p = 0.014) e cisplatino (p = 0.006) e hanno completato il trattamento in percentuale minore (p = 0.03). Per quanto concerne la tollerabilità, non è stata riportata alcuna differenza in tossicità, ospedalizzazione o morti tossiche tra i giovani e gli anziani. Un altro dato retrospettivo deriva da una "pooled analysis" condotta sui dati individuali dei 4.584 pazienti inclusi nella metanalisi LACE [157]. I pazienti sono stati suddivisi in tre gruppi in base alle seguenti fasce di età: 3.269 giovani (71% con età < 65 anni), 901 pazienti con età intermedia (20% con età tra 65 e 69 anni), e 414 anziani (9% con età > 70 anni). L'HR di mortalità è stato per i giovani dello 0.86, per la categoria intermedia 1.01, e per gli anziani 0.90. L'HR per la sopravvivenza libera da eventi è stato per i giovani 0.82, per la categoria intermedia 0.90, e per gli anziani 0.87. La percentuale di pazienti anziani che sono deceduti per cause non correlate al NSCLC è stata più elevata (12% nei giovani, 19% nella categoria intermedia, 22% negli anziani; p < .0001). Anche in questa analisi non è stata riscontrata alcuna differenza in tossicità e gli anziani hanno ricevuto meno chemioterapia [157]. Alla luce di questi dati si conferma che la chemioterapia adiuvante a base di cisplatino non dovrebbe essere preclusa agli anziani con NSCLC radicalmente operato solo in base all'età cronologica anche se rimangono perplessità sulla tollerabilità di schemi chemioterapici aggressivi contenenti platino in pazienti anziani nella pratica clinica.

Va comunque considerato che i dati nella popolazione ≥75 anni sono molto esigui essendo pochi i pazienti con tale età inseriti negli studi clinici e che la scelta di effettuare il trattamento deve essere presa sempre con grande cautela. Ad ogni modo i dati oggi disponibili sulla chemioterapia adiuvante del NSCLC dei pazienti anziani sono solo retrospettivi e solo studi randomizzati prospettici potranno fornire risultati adeguati.

Un'analisi condotta su 1.507 pazienti inclusi in studi randomizzati di terapia neoadiuvante ha evidenziato un vantaggio in sopravvivenza a favore della chemioterapia del 12% (HR 0.88, intervallo di confidenza al 95% 0.76-1.01, p = 0.07), equivalente ad un miglioramento assoluto in sopravvivenza a 5 anni del 5% [158]. Purtroppo, ad oggi, non sono disponibili studi clinici di chemioterapia neoadiuvante nei pazienti anziani affetti da NSCLC. Questo tipo di approccio terapeutico essendo generalmente meglio tollerato di quella adiuvante potrebbe essere particolarmente interessante proprio nei pazienti anziani che potrebbero sopportarla meglio rispetto alla terapia standard post-operatoria.

Un dato interessante è emerso dalla metanalisi di Auperin et al. che, confermando in otre 1200 pazienti il beneficio del trattamento concomitante rispetto a quello sequenziale con un aumento

della sopravvivenza del 4.5% a 5 anni [159], non trova nell'età una discriminante nell'ottenimento del beneficio che quindi viene confermato anche nella popolazione anziana. Sempre più emerge quindi l'osservazione che non tanto l'età anagrafica quanto quella cosiddetta biologica sia uno dei fattori che deve orientare il clinico nella proposta del miglior approccio terapeutico. Pertanto, non sono al momento disponibili dati certi su quale possa essere il migliore approccio terapeutico nei pazienti anziani con NSCLC allo stadio IIIB. Anche se l'associazione risulta più efficace, l'approccio chemio-radioterapico sequenziale e la sola radioterapia potrebbero essere valide alternative nei casi in cui vi sono preoccupazioni sulla tollerabilità di un trattamento chemioterapico.

Nello studio di fase III PACIFIC, per tutti i sottogruppi considerati, inclusa l'età essendo stati arruolati pazienti con un range fino a 90 anni, i risultati sono stati a favore del consolidamento con durvalumab [160]. Ovviamente occorre molta attenzione nel selezionare pazienti ultrasettantenni da sottoporre ad un trattamento così intensivo.

RACCOMANDAZIONI

- *Per i pazienti anziani affetti da NSCLC allo stadio II-IIIA radicalmente operato, con un buon performance status, in assenza di patologia concomitanti maggiori, con un buon recupero post-operatorio la chemioterapia adiuvante con regimi a base di sale di platino è una opzione terapeutica.*

  LIVELLO DI EVIDENZA **III**
  GRADO DI RACCOMANDAZIONE **B**

- *Per i pazienti anziani affetti da NSCLC allo stadio IIIA, con un buon performance status, in assenza di patologie concomitanti maggiori, la chemioterapia neoadiuvante con regimi a base di sale di platino rappresenta una opzione terapeutica.*

  LIVELLO DI EVIDENZA **IV**
  GRADO DI RACCOMANDAZIONE **C**

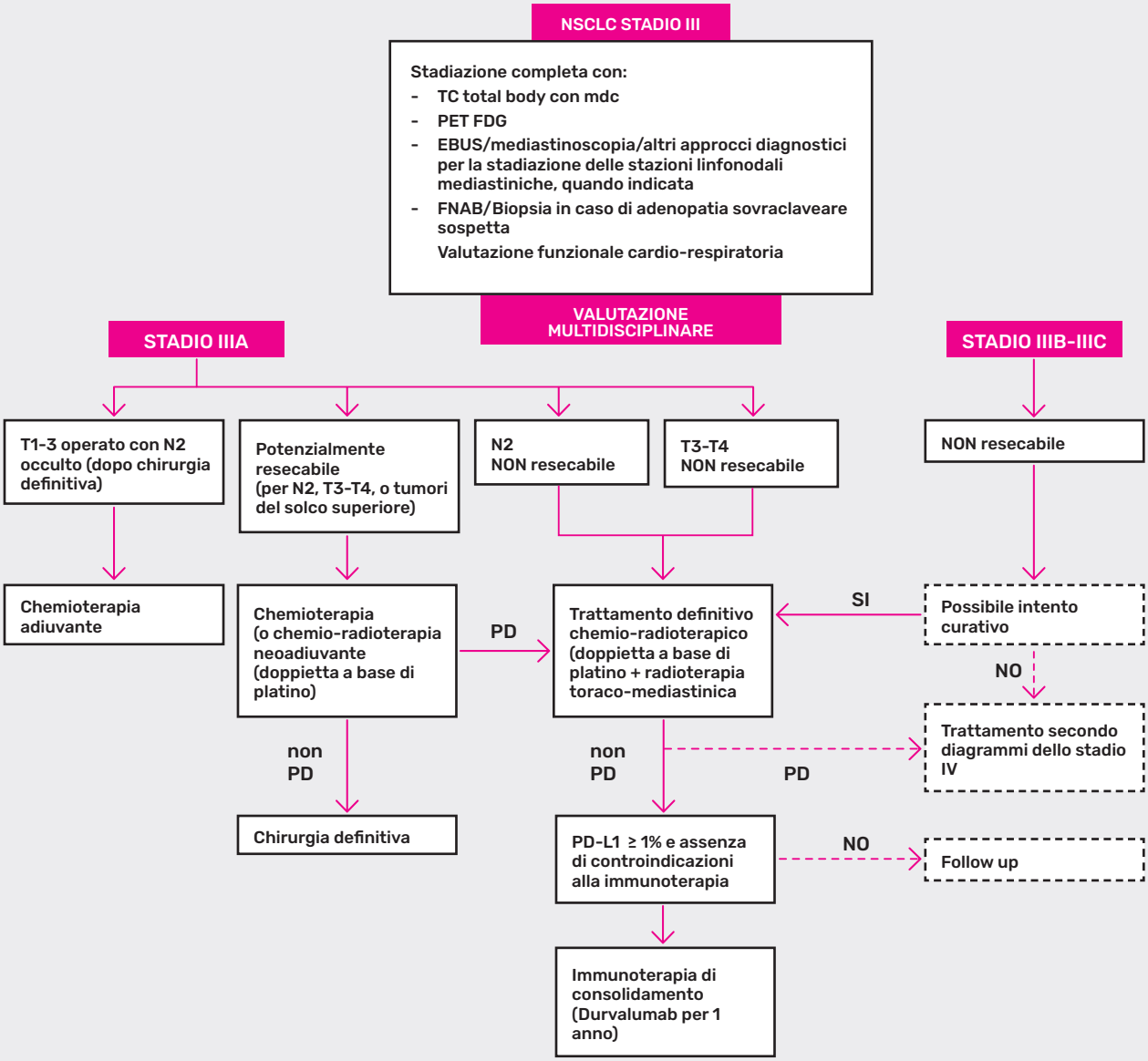
- *Per i pazienti anziani affetti da NSCLC allo stadio IIIB-C, con un buon performance status, in assenza di patologie concomitanti maggiori, è raccomandata la chemioradioterapia sequenziale o, in casi estremamente selezionati, concomitante.*

  LIVELLO DI EVIDENZA **IV**
  GRADO DI RACCOMANDAZIONE **C**

- *Per i pazienti anziani (età ≥ 65 anni) affetti da NSCIC allo stadio IIIA non operabile/IIIB-C con PD-L1 ≥1%, con un buon performance status, in assenza di patologie concomitanti maggiori ed in cui l'immunoterapia non è controindicata, il trattamento di consolidamento con durvalumab dopo chemio-radioterapia (almeno 2 cicli di chemioterapia) a dosi radicali è raccomandato.*

  LIVELLO DI EVIDENZA **III**
  GRADO DI RACCOMANDAZIONE **B**

ALGORITMO DI TRATTAMENTO NEL NSCLC LOCALMENTE AVANZATO



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