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83P - Pathologic complete response after neoadjuvant chemoimmunotherapy in resectable non-small cell lung

cancer (NSCLC): a systematic review and pooled analysis

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Introduction

- Early results evaluating immunotherapy (IO)-based neoadjuvant strategies for NSCLC have been promising, with an emphasis on pathologic endpoints (i.e. CheckMate-816, NeoStar, etc) ¹⁻²
- Several recent studies in NSCLC suggest a strong association between pathologic complete response (pCR) and survival ³
- Given the increasing number and variety of regimens, studies defining collective pathologic complete response (pCR) rates are needed for future clinical trial design and eventual practice.
- Comparing these novel neoadjuvant approaches to FDA approved chemotherapy (chemo) regimens can also provide insight into efficacy and utility.
- We sought to compare rates of pCR based on various neoadjuvant treatment options, along with clinically relevant subgroup analysis.

Methods

- MEDLINE and SCOPUS databases were searched to identify articles and abstracts, published before 2021/11, of prospective clinical trials reporting pCR and major pathologic response (MPR) of neoadjuvant IO, chemo and chemoimmunotherapy (chemo+IO) regimens in resectable NSCLC.
- Random effect meta-analysis was conducted to estimate pooled pCR and MPR rates of each regimen, and meta-regression was used to evaluate differences in pCR between regimens, by adjusting for stage (I/II vs. III). Sensitivity analyses were conducted to assess impact of cross-study variations.
- 41 total trials with a total of 2964 patients were included, including 19 IObased trials, and 22 chemo-based trials. Of the IO-based trials, they were further broken down into IO-only vs chemo+IO regimens. 2 chemo-only control arms from IO RCTs were included under chemo analysis.

Table 1: Study search eligibility criteria using PICOS focused tool.

PICOS	Eligibility
Population	Resectable NSCLC (stage I-III)
Intervention	Neoadjuvant chemotherapy, IO, chemo+IO without XRT
Outcomes	pCR, OS, EFS
Design	RCTs, prospective trials, excluding observational/retrospective reports
Restriction	English language, year 2000 or >, platinum based chemo regimens





pCR Resected pts 0.00 [0.00; 0.17] 0.00 [0.00; 0.13] 12579093 J Thor CV Surg $\begin{array}{c} 2.0\%\\ 3.8\%\\ 5.5\%\\ 5.8\%\\ 18.4\%\\ 5.7\%\\ 1.8\%\\ 0.8\%\\ 1.5\%\\ 1.5\%\\ 1.5\%\\ 1.5\%\\ 3.7\%\\ 9.5\%\\ 3.7\%\\ 0.5\%\\ 4.3\%\\ 3.7\%\\ 0.4\%\\ 0.4\%\\ 0.4\%\\ 0.4\%\\ 0.4\%\\ 0.2\%\\ \end{array}$ $\begin{array}{c} 3.8\% \\ 5.0\% \\ 5.9\% \\ 5.9\% \\ 7.3\% \\ 5.7\% \\ 3.8\% \\ 2.0\% \\ 3.8\% \\ 2.6\% \\ 1.6\% \\ 5.1\% \\ 1.6\% \\ 5.1\% \\ 1.2\% \\ 0.9\% \\ 1.2\% \\ 0.7\% \\ 1.1\% \\ 7.1\% \\ 0.7\% \end{array}$ 29572004 Lung Cancer 0.00 [0.00; 0.10] 0.03 [0.00; 0.10] 0.03 [0.01; 0.06] 24419420 JTO 18166839 JTO 17544497 Lancet 253 22124104 JCO 18303436 JTO 110 106 0.05 [0.01; 0.10] 18728643 BJC 0.05 [0.01; 0.17 0.06 [0.00; 0.27] 0.06 [0.01; 0.19] 0.06 [0.01; 0.18] 12448663 Invest 11870504 BJC 15603860 Lung Cancel 0.06 [0.01; 0.18] 0.07 [0.01; 0.22] 0.07 [0.00; 0.32] 0.09 [0.05; 0.13] 0.06 [0.04; 0.10] 11844608 Lung Cancer 30 11870532 BJC 23735703 Eur J Cancer 257 252 152 181 167 23735703 Eur J Cancer 20231678 JCO 0.10 0.06; 0.16 20516435 JCO 0.10 10.08 0.16 11773176 JCO 0.11 0.07:0.17 17409842 JTO 0.14 [0.05; 0.29 14644524 Lung Cancer 21847062 JTO 0.14 [0.03; 0.36 0.17 [0.04; 0.41 21 16622435 BJC 75 0.19 0.11.0.29 0.24 [0.10; 0.44] 14534888 Cancer 29 179 Abstract AACR Abstract ESMO 0.15 [0.02: 0.45 Common effect model 0.05 [0.04: 0.06] 100.0% Random effects model 0.06 [0.04; 0.08 Heterogeneity: I² = 62%, τ² = 0.0010, p Overall pCR rate=6% 0 0.1 0.2 0.3 0.4

Figure 2: Forest plot diagrams summarizing results from proportional meta-analysis for (a) IO-based regimens and (b) chemotherapy regimens



Figure 3: Results of meta-regression analysis conducted to study the effects of (a) regimen type and (b) stage (I/II vs. III) on rate of pCR

Conclusions

- Neoadjuvant chemo+IO achieved highest rates of pCR compared to chemo alone (p < 0.0001)- regardless of patient stage- while similar trends were not seen for either IO alone or chemo.
- There was a numerical difference in pCR between chemo and IO, however this did not reach statistical significance (p=0.34).
- Stage III patients trended toward increased pCR% regardless of regimen (p=0.09)
- These pooled rates of pCR may serve as useful benchmarks to inform future neoadjuvant trial design, prioritization and patient management.

References

1 Forde et al. AACR 2021 (oral presentation); 2 Cascone T, et al. *Nat Med* 2021; 3 Waser N, et al. ESMO 2020 (poster)