Long-Term Extrapolation of Overall Survival (OS) and Progression-Free Survival (PFS) for the LUNAR Trial in Metastatic Non-Small Cell Lung Cancer (NSCLC) Following Progression on Platinum-Based Therapy

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Objective

Objective:
To estimate overall survival (OS) and progression-free survival (PFS) over a lifetime horizon in patients with metastatic non-small cell lung cancer (NSCLC) following progression on or after platinum-based therapy, based on data from the LUNAR trial[1].

Study Aim:
To compare the effects of Tumor Treating Fields (TTFields) therapy added to either an immune checkpoint inhibitor (ICI) or docetaxel versus ICI or docetaxel alone.

Key Takeaways

- The extrapolation method offers reliable long-term predictions for OS and PFS in patients with NSCLC treated with TTFields therapy.
- These projections are essential for evaluating the potential long-term benefits and costs of TTFields therapy.
- The use of accurate and clinically relevant statistical measures must be confirmed with expert opinions to provide credible long-term outcome predictions.
- The findings are valuable for assessing the cost-effectiveness of TTFields therapy and supporting healthcare decision-making.

LUNAR Trial Overview

- The **LUNAR trial** is a **Phase 3 clinical study** designed to evaluate the effectiveness of **TTFields** therapy concomitant with ICI or docetaxel for patients with **metastatic NSCLC** who have been previously treated with **platinum-based chemotherapy**.
- The trial showed that adding **TTFields** therapy to ICI or docetaxel for metastatic **NSCLC** significantly improved OS for patients after platinum-based chemotherapy[1]. Key results include:
  1) **3.3-month improvement in median survival** (13.2 vs. 9.9 months) with TTFields therapy plus ICI or docetaxel.
  2) **7.7-month improvement** when TTFields therapy was added to an ICI (18.5 vs. 10.8 months).
  3) **No additional systemic toxicities** were observed when TTFields therapy was added to an ICI or docetaxel.
  4) **First significant survival improvements in metastatic NSCLC** in over eight years, with data submitted for and approved by the FDA[2].

Methods

- In the LUNAR trial, short follow-up times (10.6 months for TTFields therapy + ICI or docetaxel, and 9.5 months for ICI or docetaxel alone) required extrapolation to estimate long-term outcomes[1].
- Kaplan-Meier analysis was used to track OS up to 36 months and PFS for six weeks across the four treatment groups: TTFields therapy + docetaxel, docetaxel alone (Figure 1 and 3), TTFields therapy + ICI, and ICI alone (Figure 2 and 4).
- To project survival beyond the observed period, parametric models including exponential, Weibull, log-normal, log-logistic, generalized gamma, and gamma—were applied, with model selection based on the Akaike Information Criterion (AIC), Bayesian information criterion (BIC), and clinical plausibility as shown on Tables 1 and 2.
- Results were confirmed by expert opinion.
- This approach ensured valid long-term survival estimates, supporting TTFields therapy's effectiveness evaluation.

Results

Overall Survival (OS):
OS data were capped at 36 months due to a significant reduction in patient numbers. For extrapolation, log-normal distributions were used for TTFields therapy + docetaxel, gamma distributions for docetaxel alone, generalized gamma for TTFields therapy + ICI, and log-normal for ICI alone.

Results (continued)

Progression-Free Survival (PFS):
PFS data were limited to six weeks, consistent with initial radiographic assessments in NSCLC studies. Gamma distributions were used for TTFields therapy + docetaxel, while exponential distributions were applied for TTFields therapy + ICI.

OS	TTFields + Docetaxel		TTFields +ICIs	
Distribution	AIC	BIC	AIC	BIC
Exponential	542	544	410	493
Weibull	542	546	411	484
Log-Normal	544	548	405	484
Log-Logistic	564	569	416	501
Generalized Gamma	542	549	407	487
Gompertz	792	796	603	559
Gamma	541	546	412	483

Table 1: AIC and BIC Scores for Overall Survival Model Selection Across Treatment Arms

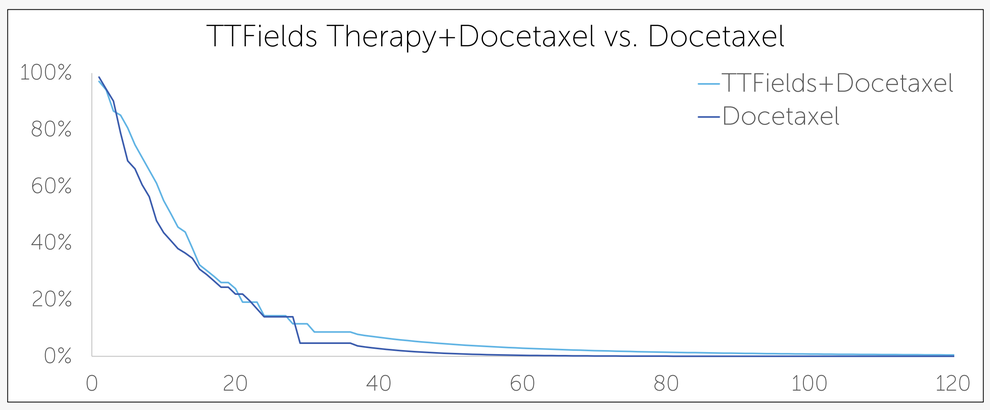

Figure 1: Overall Survival TTFields + Docetaxel vs. Docetaxel

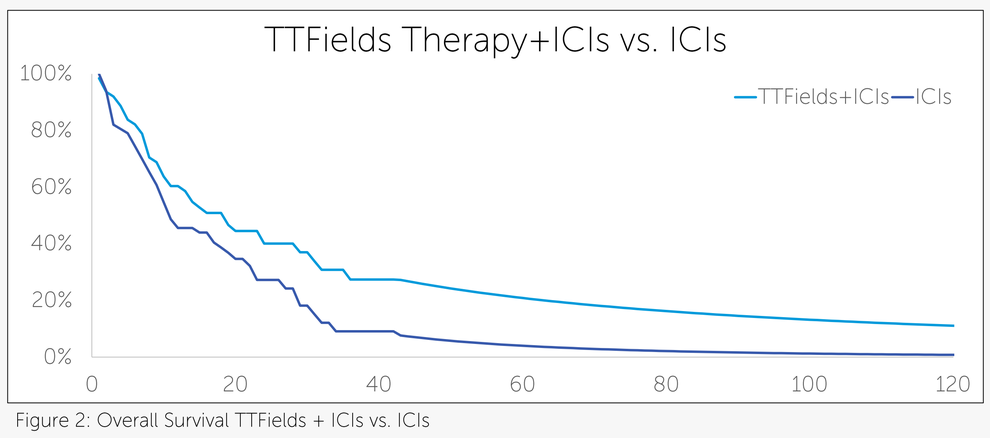

Figure 2: Overall Survival TTFields + ICIs vs. ICIs

PFS	TTFields + Docetaxel		TTFields +ICIs	
Distribution	AIC	BIC	AIC	BIC
Exponential	490	493	395	397
Weibull	480	484	396	400
Log-Normal	479	484	389	393
Log-Logistic	496	501	403	407
Generalized Gamma	480	487	389	395
Gompertz	555	559	426	431
Gamma	479	483	396	401

Table 2: AIC and BIC Scores for Progression-Free Survival (PFS) Model Selection Across Treatment Arms

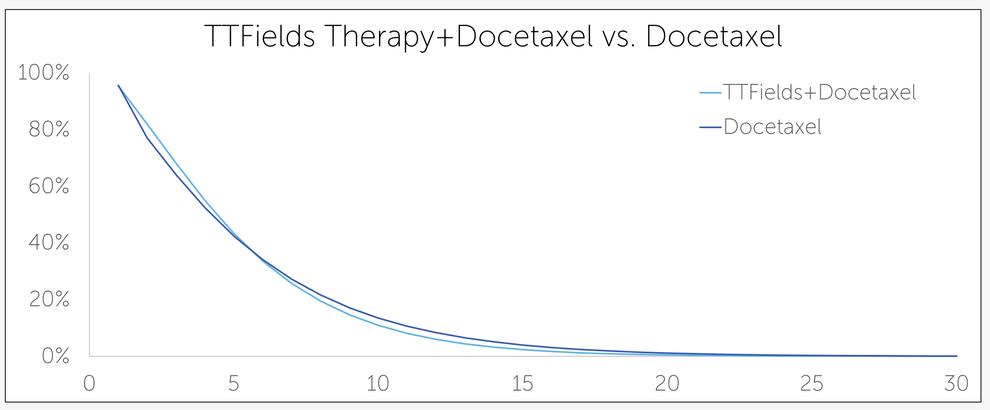

Figure 3: Progression-free Survival TTFields + Docetaxel vs. Docetaxel

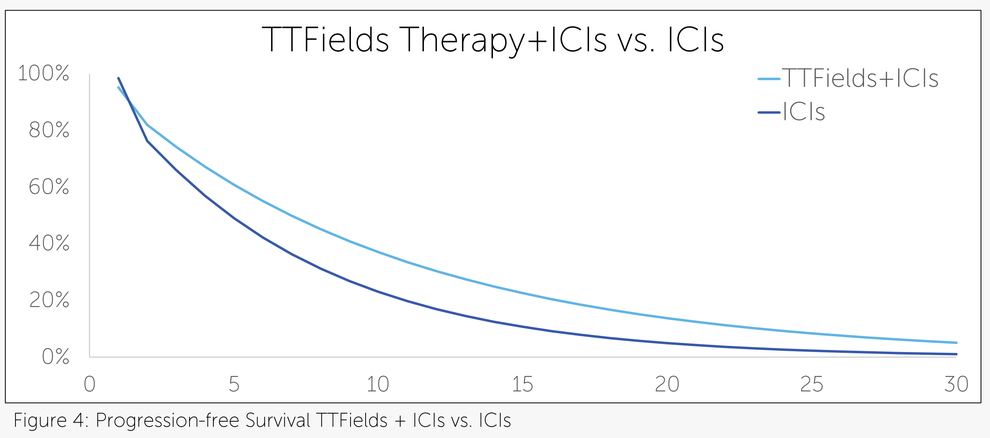

Figure 4: Progression-free Survival TTFields + ICIs vs. ICIs

References: 1) Leal T, Kotecha R, Ramlau R, et al. Tumor Treating Fields therapy with standard systemic therapy versus standard systemic therapy alone in metastatic non-small-cell lung cancer following progression on or after platinum-based therapy (LUNAR): a randomised, open-label, pivotal phase 3 study. *Lancet Oncol*. 2023;24(9):1002–1017. 2) Novocure Press Release. October 15, 2024. Available at: https://www.novocure.com/fda-approves-novocures-optune-lua-for-the-treatment-of-metastatic-non-small-cell-lung-cancer/

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