Impact of BMI on TTFields in Patients with mNSCLC: Post-hoc Analysis from the Phase 3 LUNAR Study and Simulation Model Data

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Introduction

- Tumor Treating Fields (TTFields) are electric fields that disrupt processes critical for cancer cell viability and tumor progression[1–3]
  - TTFields have an anti-mitotic effect with downstream enhanced antitumor immunity[1–3]
- TTFields therapy is delivered non-invasively via a portable medical device using 2 pairs of arrays placed on the torso (**Figure 1**) or scalp
- TTFields therapy is approved for glioblastoma by the FDA and CE-marked for WHO grade 4 glioma in the EU, as well as for pleural mesothelioma[4,5]
- The pivotal, phase 3 LUNAR trial (NCT02973789) in patients with metastatic non-small cell lung cancer progressing after platinum-based chemotherapy demonstrated that TTFields therapy plus an immune checkpoint inhibitor (ICI) or docetaxel (DTX) led to a statistically significant and clinically meaningful improvement in median overall survival (OS) compared to an ICI or DTX alone (median OS 13.2 vs 9.9 months; hazard ratio [HR]: 0.74; 95% confidence interval, 0.56–0.98; *P*=0.035)[6]
- Since TTFields intensity (which is critical for effectiveness) can be impacted by tissue conductivity,[7] it is relevant to evaluate the effect of body mass index (BMI) on the delivery of TTFields to the lungs

Figure 1. The TTFields device components and example array layout

Example array layout for the torso
Image shows an actor and not a patient

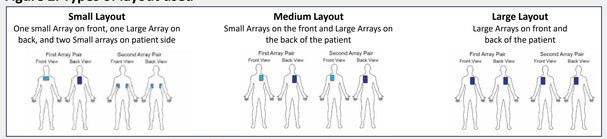
Aim

- To evaluate the effect of BMI on delivery of TTFields to the lung, efficacy, and safety

Methods

- This *post-hoc* analysis of the LUNAR study assessed efficacy and safety according BMI subgroups: low (<25 kg/m^2) vs high (≥25 kg/m^2)
  - Classifications were determined by using WHO recognized criteria[8]
- TTFields intensity and distribution was evaluated using 2 array sizes, and 3 layouts (small, medium, and large) in computerized phantom models categorized as healthy (BMI 22 kg/m^2), overweight (BMI 26 kg/m^2), and obese (BMI 30 kg/m^2) (**Figure 2**)

Figure 2. Types of layout used



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Results

- Of 276 randomized patients, 259 (94%) had BMI data available
  - Of the 140 patients in the low BMI group, 12 (5%) were underweight (<18.5 kg/m^2)
  - Of the 119 patients in the high BMI group, 42 (16%) were obese (≥30.0 kg/m^2)

Baseline demographics and clinical characteristics

- Baseline demographics and clinical characteristics were similar between subgroups (**Table 1**)

Table 1. Baseline demographics and clinical characteristics

	BMI <25 kg/m^2 (n=140)*		BMI ≥25 kg/m^2 (n=119)	
	TTFields therapy + ICI/DTX	ICI/DTX	TTFields therapy + ICI/DTX	ICI/DTX
n, (%)	81 (57.9)	59 (42.1)	50 (42.0)	69 (58.0)
Age (years), median (range)	63.0 (43–85)	64.0 (35–85)	65.0 (36–81)	65.0 (22–86)
Sex, male, n (%)	56 (69.1)	34 (57.6)	33 (66.0)	47 (68.1)
ECOG PS score, n (%)				
0	20 (24.7)	16 (27.1)	18 (36.0)	21 (30.4)
1	57 (70.4)	41 (69.5)	30 (60.0)	46 (66.7)
2	4 (4.9)	2 (3.4)	2 (4.0)	2 (2.9)
Smoking history, n (%)				
Never smoked	15 (18.5)	12 (20.3)	5 (10.0)	8 (11.6)
Current smoker	21 (25.9)	15 (25.4)	14 (28.0)	13 (18.8)
Former smoker	45 (55.6)	32 (54.2)	31 (62.0)	48 (69.6)
Histological type, n (%)				
Non-squamous	45 (55.6)	34 (57.6)	29 (58.0)	36 (52.2)
Squamous	36 (44.4)	25 (42.4)	21 (42.0)	33 (47.8)
Previous lines of systemic therapy†, n (%)				
1	71 (87.7)	56 (94.9)	47 (94.0)	61 (88.4)
2	6 (7.4)	3 (5.1)	2 (4.0)	6 (8.7)
Liver metastasis, n (%)	14 (17.3)	7 (11.9)	7 (14.0)	13 (18.8)
Brain metastasis, n (%)	0	1 (1.7)	0	1 (1.4)

*One patient randomly assigned to TTFields therapy with standard therapy instead received standard therapy alone. †A small number of patients received more than two previous lines of systemic therapy. BMI, body mass index; DTX, docetaxel; ECOG PS, Eastern Cooperative Oncology Group performance status; ICI, immune checkpoint inhibitor; TTFields, Tumor Treating Fields

Treatment exposure

- Daily usage of TTFields therapy was comparable across the BMI subgroups (**Table 2**)

Table 2. Treatments received

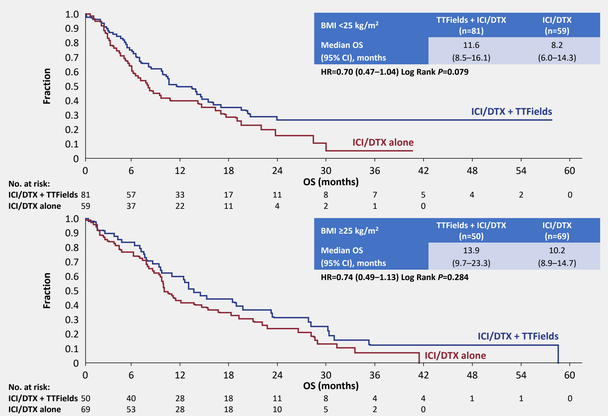
	BMI <25 kg/m^2				BMI ≥25 kg/m^2			
	TTFields therapy + ICI (n=34)	ICI (n=33)	TTFields therapy + DTX (n=46)	DTX (n=27)	TTFields therapy + ICI (n=33)	ICI (n=31)	TTFields therapy + DTX (n=17)	DTX (n=38)
Duration of ICI/DTX therapy								
Median (range), weeks	9.0 (1–69)	6.0 (1–70)	5.0 (1–20)	4.0 (2–27)	11.0 (1–92)	5.0 (2–60)	5.0 (1–13)	6.0 (1–27)
TTFields therapy								
Duration, median (range), weeks	17.4 (0.3–160.1)	NA	14.1 (0.4–52.4)	NA	13.9 (0.7–201.1)	NA	11.6 (0.1–162.6)	NA
Daily usage, median, %	55.5	NA	56.0	NA	59.7	NA	60.1	NA
Patients with >75% (≥18 h) average daily use, n (%)	6 (17.6)	NA	10 (21.7)	NA	7 (21.2)	NA	6 (35.3)	NA
Patients with ≥50% (≥12 h) average daily use, n (%)	21 (61.8)	NA	28 (60.9)	NA	19 (57.6)	NA	11 (64.7)	NA

BMI, body mass index; DTX, docetaxel; ICI, immune checkpoint inhibitor; NA, not applicable; TTFields, Tumor Treating Fields

Efficacy

- TTFields therapy with ICI/DTX showed an OS benefit vs ICI/DTX, regardless of BMI
- There was no significant difference in OS benefit for TTFields therapy between BMI subgroups (HR=0.99 [0.64–1.51]; Log Rank *P*=0.88) (**Figure 3**)
- There was no significant statistical interaction between BMI subgroups, treatment arm, and OS (*P*=0.36)

Figure 3. OS



BMI, body mass index; CI, confidence interval; DTX, docetaxel; HR, hazard ratio; ICI, immune checkpoint inhibitor; OS, overall survival; TTFields, Tumor Treating Fields

Safety and tolerability

- The overall incidence of skin device-related adverse events (AEs) was similar in both low and high BMI subgroups (**Table 3**)
- Most (95.4%) device-related AEs were mild or moderate
  - There were only 6 (4.6%) grade 3 device-related AEs across the BMI subgroups; none were above grade 3 in severity[6]

Table 3. Device-related AEs

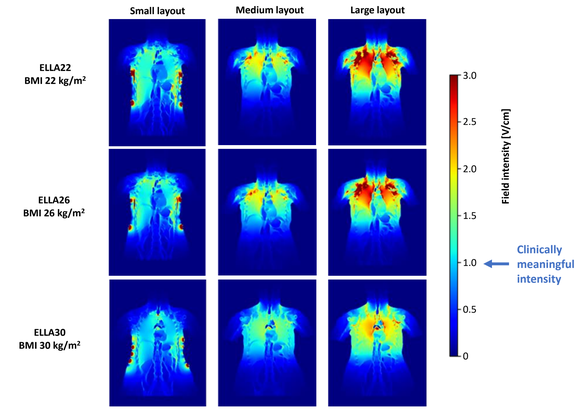
	TTFields therapy + ICI/DTX	
	BMI <25 kg/m^2 (n=80)	BMI ≥25 kg/m^2 (n=50)
Any device-related skin AE, n (%)	49 (61.3)	27 (54.0)
AE, n (%)		
Dermatitis	10 (12.5)	6 (12.0)
Skin irritation	10 (12.5)	5 (10.0)
Pruritus	9 (11.3)	4 (8.0)
Dermatitis contact	8 (10.0)	2 (4.0)
Skin toxicity	3 (3.8)	5 (10.0)
Rash	7 (8.8)	4 (8.0)
Rash maculo-papular	5 (6.3)	3 (6.0)
Device-related AE leading to discontinuation, n (%)	18 (22.5)	11 (22.0)
Device-related AE leading to death, n (%)	0	0

AE; adverse event; BMI, body mass index; DTX, docetaxel; ICI, immune checkpoint inhibitor; TTFields, Tumor Treating Fields

Simulations

- Simulation data showed that all 3 array layouts yielded clinically meaningful intensities in all lobes of the lung, regardless of BMI (**Figure 4**)

Figure 4. Images of modelled field intensities in the thorax



ELLA22, 26, and 30 are adult female computational phantom models. BMI, body mass index

Conclusions

- Simulation data suggest that TTFields can be delivered at clinically meaningful intensities in all BMI models assessed
- TTFields therapy with ICI/DTX offers improved survival vs ICI/DTX regardless of BMI
- BMI did not affect the incidence of device-related skin AEs
- Taken together, these data suggest TTFields delivery to the lungs is adequate and provides a clinical benefit for patients with varying BMI

References **1.** Mun EJ et al. *Clin Cancer Res*. 2018;24(2):266–275. **2.** Giladi M et al. *Sci Rep*. 2015;5:18046. **3.** Voloshin T et al. *Cancer Immunol Immunother*. 2020;69(7):1191–1204. **4.** Optune Gio. Instructions for Use. Novocure; US 2023. Accessed July 2024. **5.** Optune Lua. Instructions for Use for Unresectable Malignant Pleural Mesothelioma. Novocure; US 2021. Accessed July 2024. **6.** Leal T et al. *Lancet Oncol.* 2023;24:1002–1017. **7.** Giladi M et al. *Semin Oncol.* 2014;41(Suppl 6):S35–S41. **8.** Weir CB et al. BMI Classification Percentile And Cut Off Points. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan.

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