Oncology Today with Dr Neil Love — Role of PARP Inhibition in Ovarian Cancer and Recent Data with Tumor Treating Fields: A Special Dual-Focused Webinar

A CME/MOC-Accredited Virtual Event

Thursday, February 23, 2023
5:00 PM – 6:00 PM ET

Faculty

Gottfried E Konecny, MD
Chirag B Patel, MD, PhD

Moderator

Neil Love, MD

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RESEARCH TO PRACTICE

Faculty

Gottfried E Konecny, MD
Professor of Medicine and Ob/Gyn
Director, Medical Gynecologic Oncology
Division of Hematology and Oncology
David Geffen School of Medicine
University of California, Los Angeles
Los Angeles, California

Chirag B Patel, MD, PhD
Assistant Professor of Neuro-Oncology
and McNair Scholar
The University of Texas
MD Anderson Cancer Center
Neuroscience and Cancer Biology Programs
UTHealth Graduate School of Biomedical Sciences
Houston, Texas

Moderator
Neil Love, MD
Research To Practice

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ONCOLOGY TODAY

WITH DR NEIL LOVE

Role of PARP Inhibition in Ovarian Cancer

DR THOMAS HERZOG

UNIVERSITY OF CINCINNATI MEDICAL CENTER

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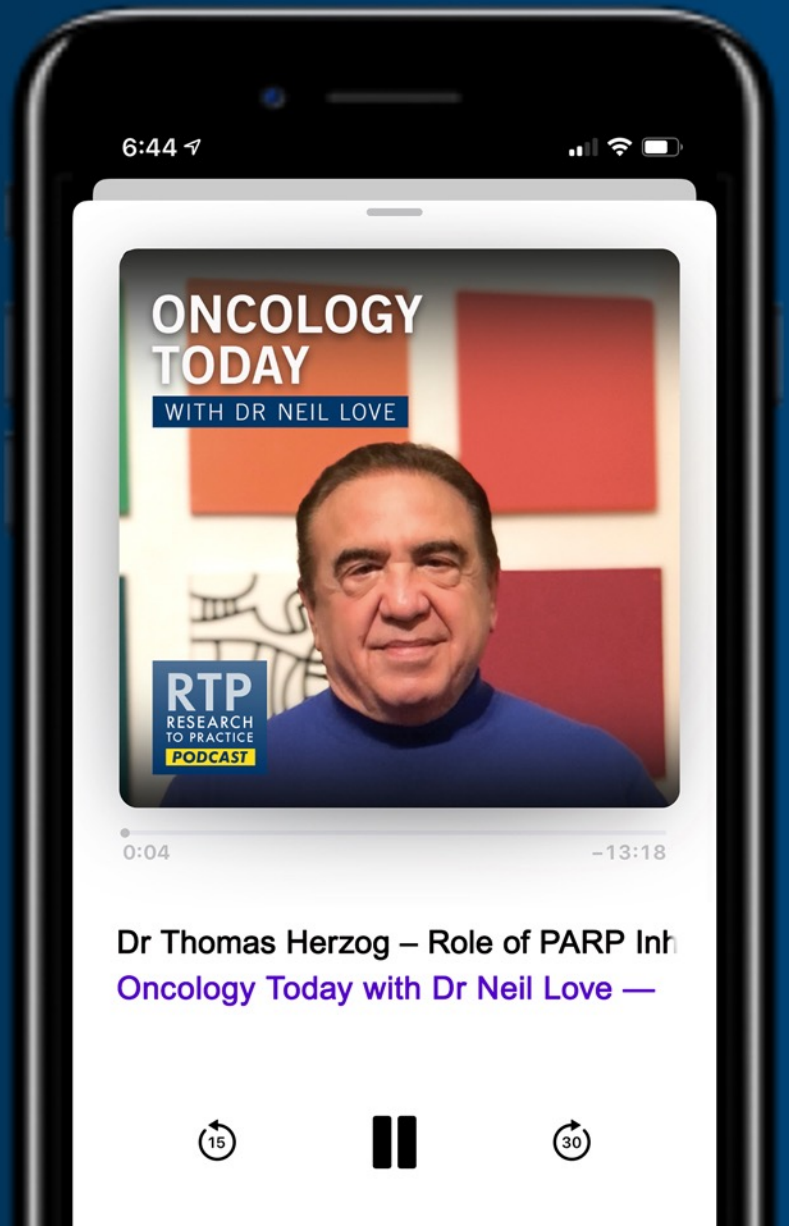

Year in Review: Clinical Investigator Perspectives on the Most Relevant New Data Sets and Advances in Oncology

A Multitumor CME/MOC-Accredited Live Webinar Series

Prostate Cancer

Wednesday, March 1, 2023
5:00 PM – 6:00 PM ET

Faculty

Tanya B Dorff, MD

A Oliver Sartor, MD

Moderator

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RTP Year in Review 2023

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Thomas Powles, MBBS, MRCP, MD

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Meet The Professor

Optimizing the Management of ER-Positive and Triple-Negative Breast Cancer

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5:00 PM – 6:00 PM ET

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Sara M Tolaney, MD, MPH

Moderator

Neil Love, MD

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Swati Vishwanathan, MD

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Optimizing the Management of Colorectal Cancer

Part 2 of a 3-Part Series

Wednesday, March 22, 2023
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John Strickler, MD

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Neil Love, MD

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Amit M Oza, MD

Richard T Penson, MD, MRCP

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Dr Love — Disclosures

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Dr Konecny — Disclosures

No relevant conflicts of interest to disclose.

Dr Patel — Disclosures

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Thank you for joining us!

CME and MOC credit information will be emailed to each participant within 5 business days.

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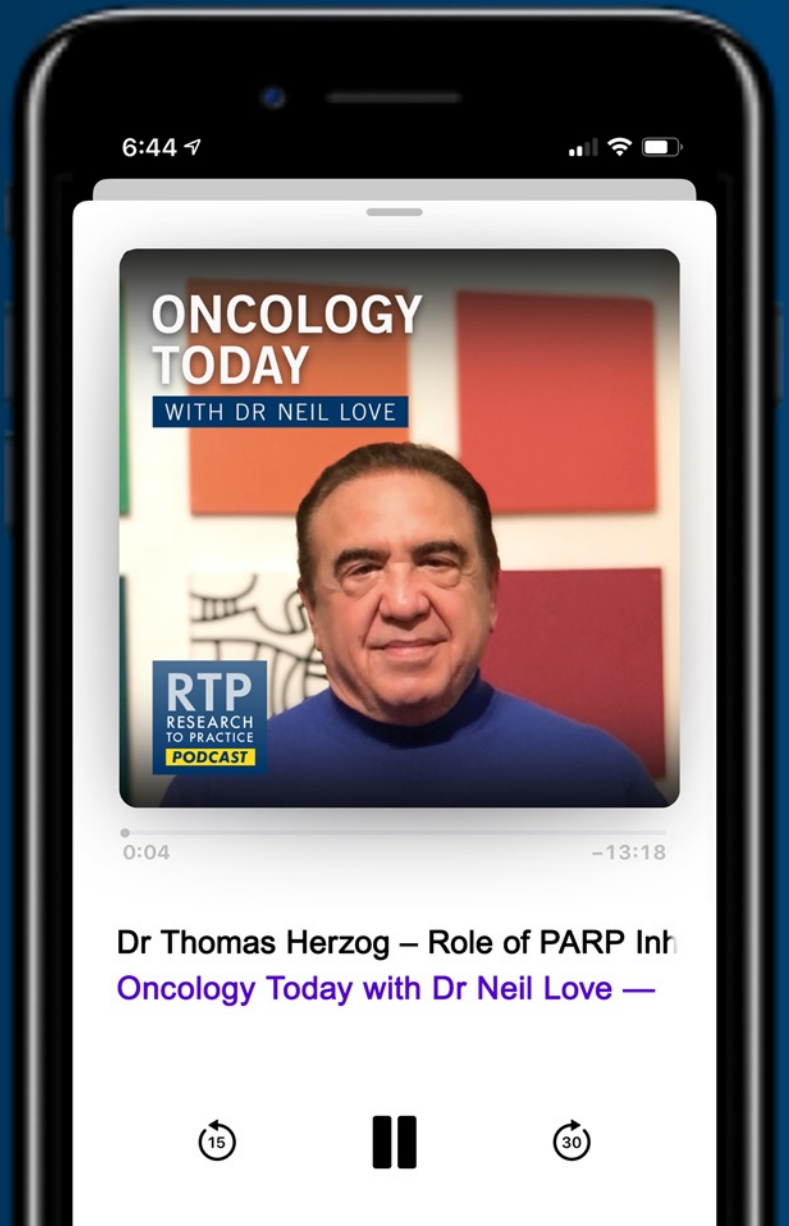

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Dr Konecny — Disclosures

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Tumor Treating Fields & Ovarian PARP

Chirag Patel, MD, PhD
Assistant Professor, Dept. of Neuro-Oncology, MD Anderson Cancer Center
Neuroscience and Cancer Biology Programs, Graduate School of Biomedical Sciences

RTP 2022 Oncology Today Live Webcast
2/23/2023

THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

McNair Scholar

Updates On PARP Inhibitors 2023

Gottfried E. Konecny
Professor of Medicine and OB/GYN
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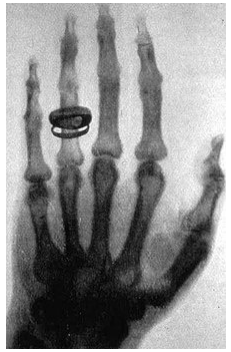
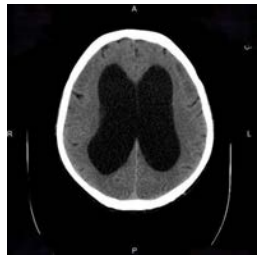
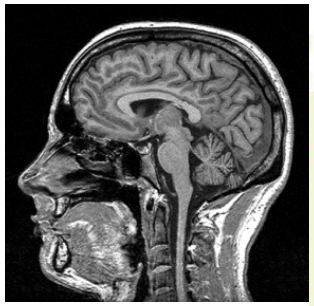
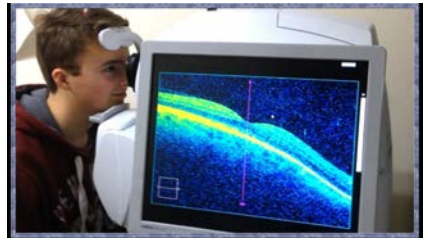
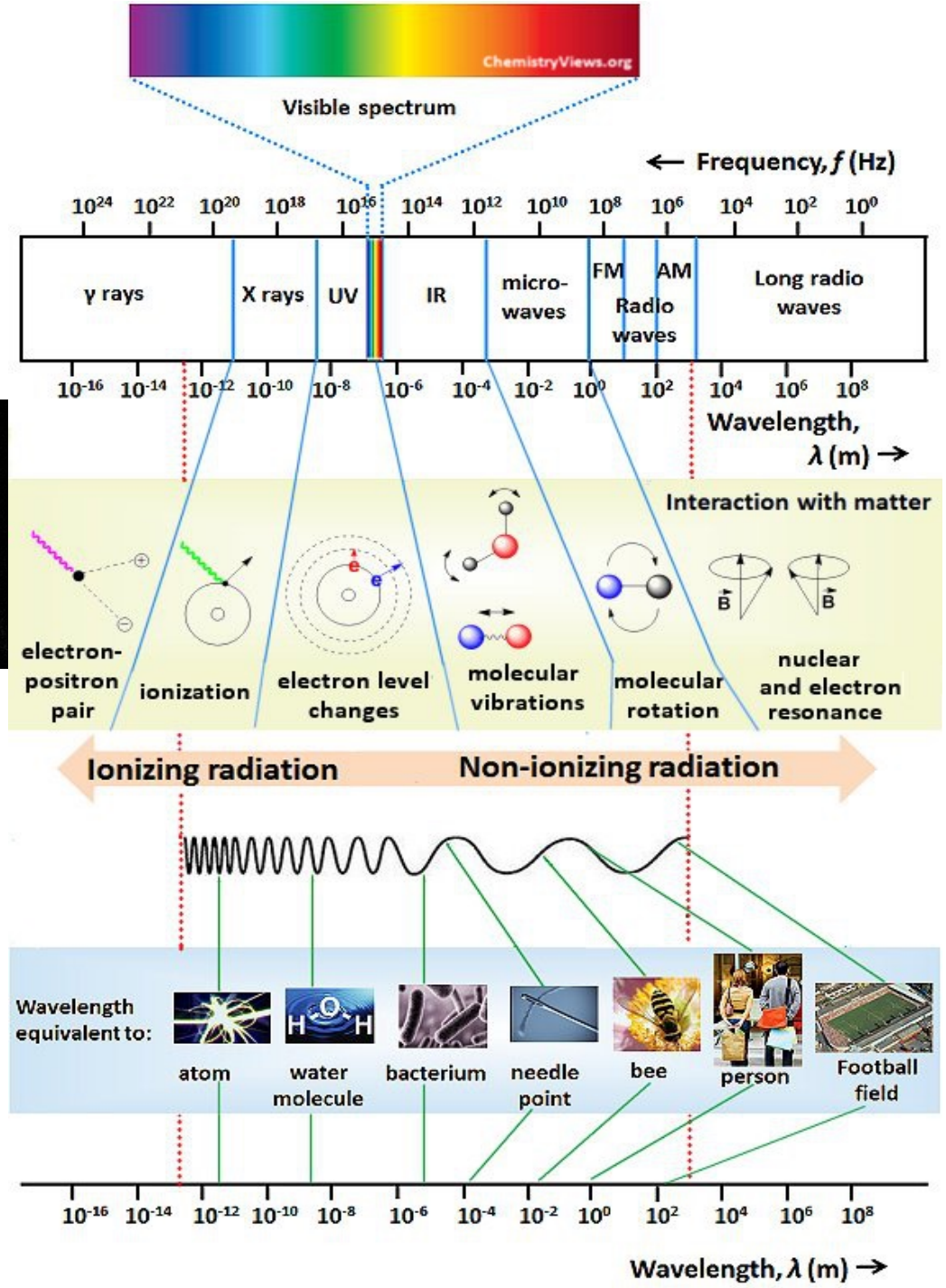
Electromagnetic Spectrum: Diagnostics





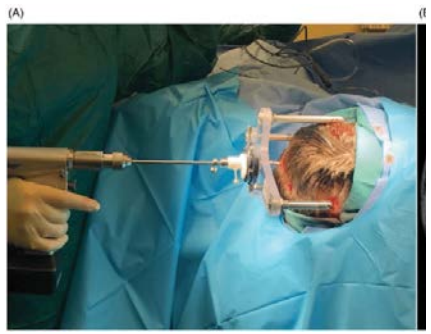


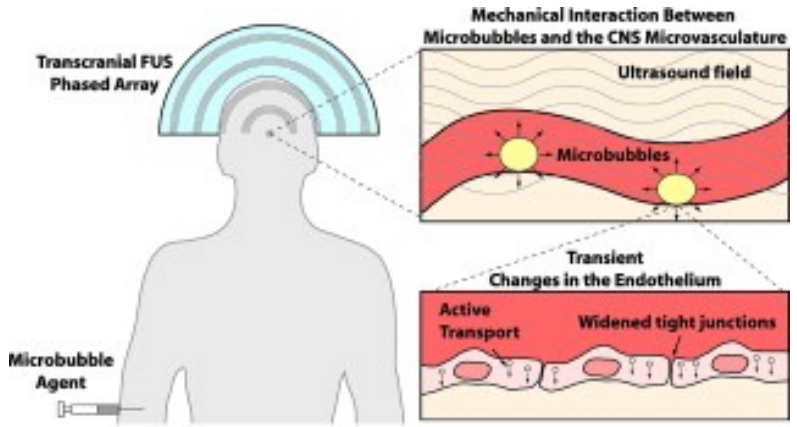




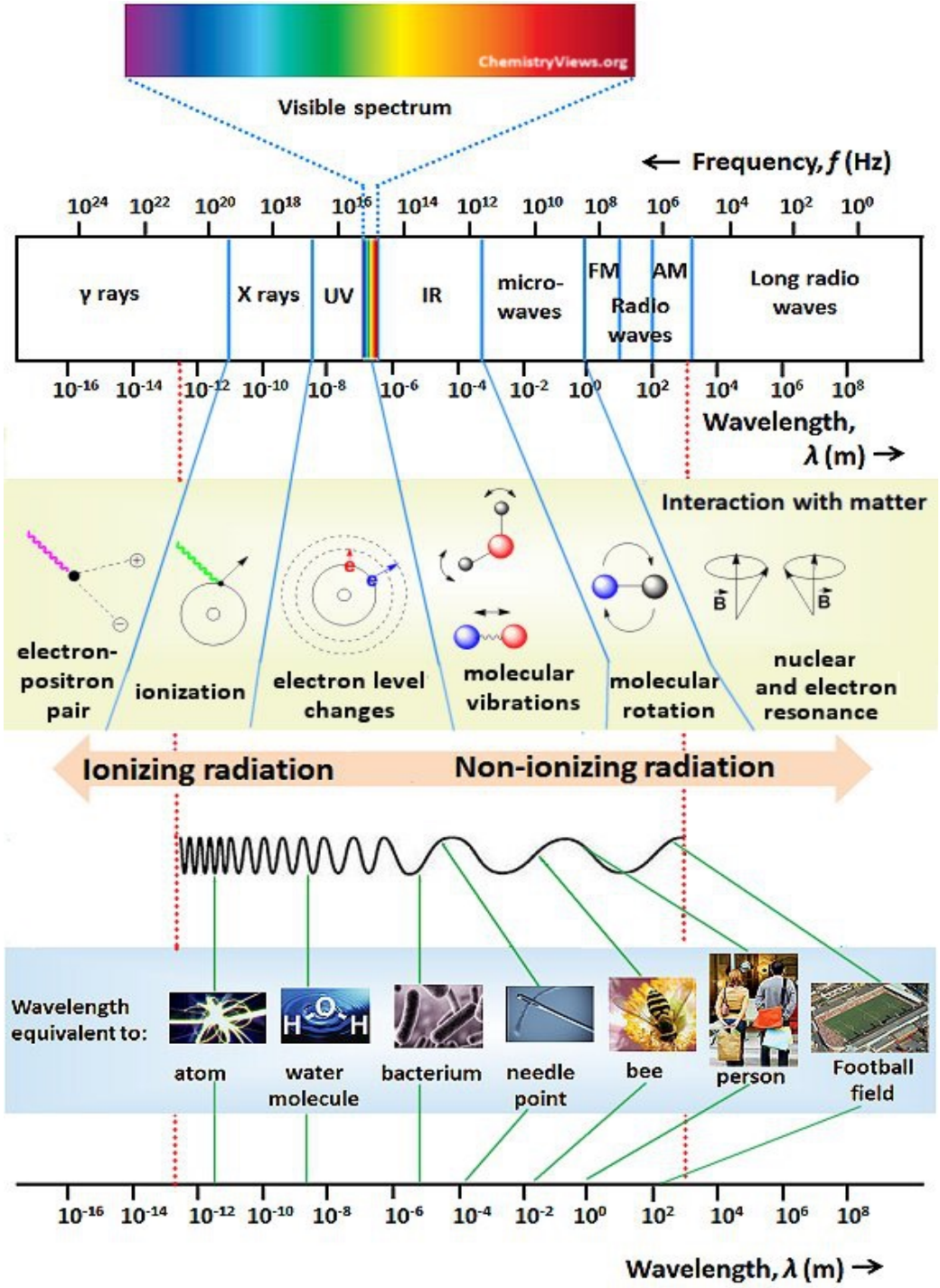
https://www.chemistryviews.org/

Electromagnetic Spectrum: Therapeutics





BBB Disruption via Focused Ultrasound and Microbubbles: Noninvasive, Transient, Targeted Drug Delivery



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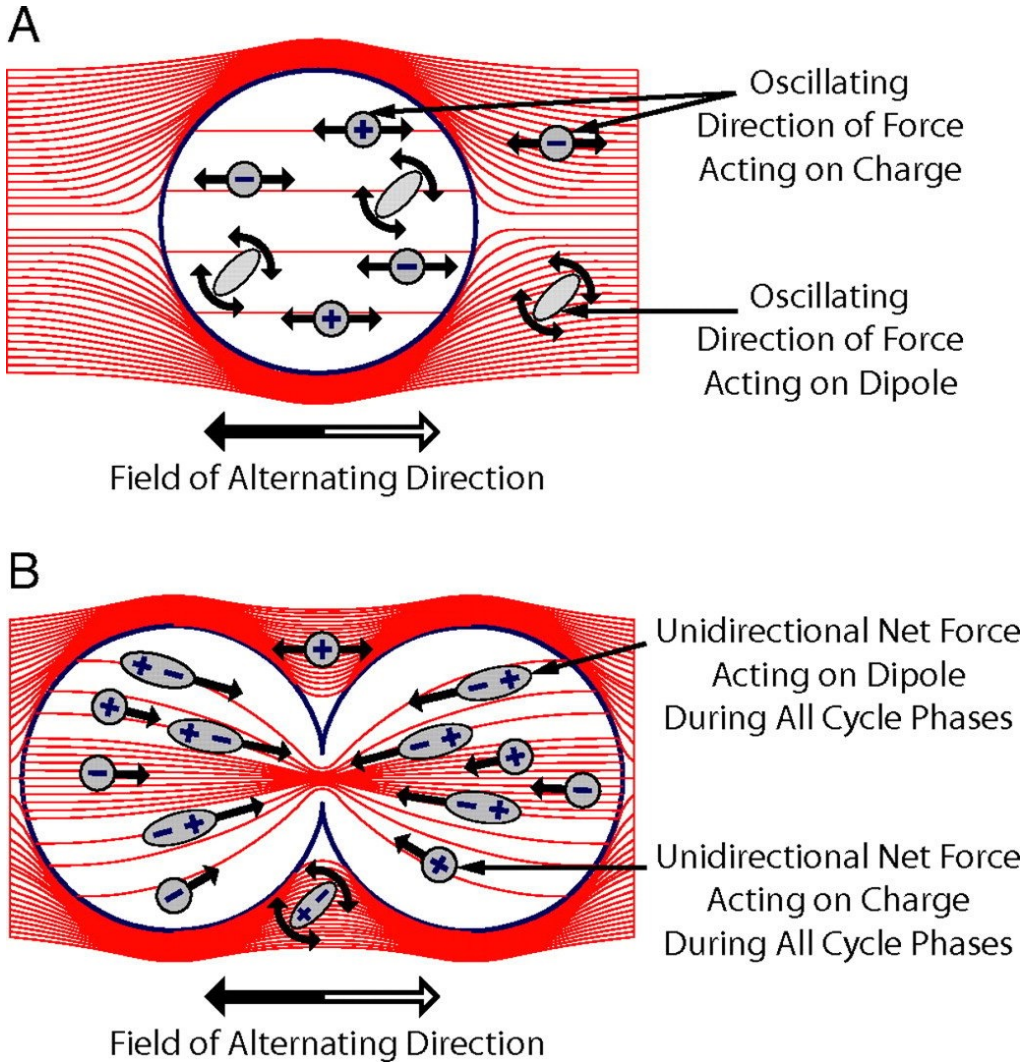
Tumor Treating Fields (TTFields)

- 100-300 kHz alternating electric fields with intensity of 1-4 V/cm



AC field distribution in and around quiescent (A) and dividing (B) cells. Inside quiescent cells, the field is uniform, and the oscillating electric forces result only in "vibration" of ions and dipoles (the forces associated with each half cycle are denoted white and gray arrows). In contrast, the nonuniform field within dividing cells (B) induces forces pushing all dipoles toward the furrow. Note that at frequencies of 0.1–1.0 MHz, the cell membrane impedance is relatively high, so only a small fraction of the currents penetrate the cells as seen from the density of lines.

Kirson et al., 2007, PNAS

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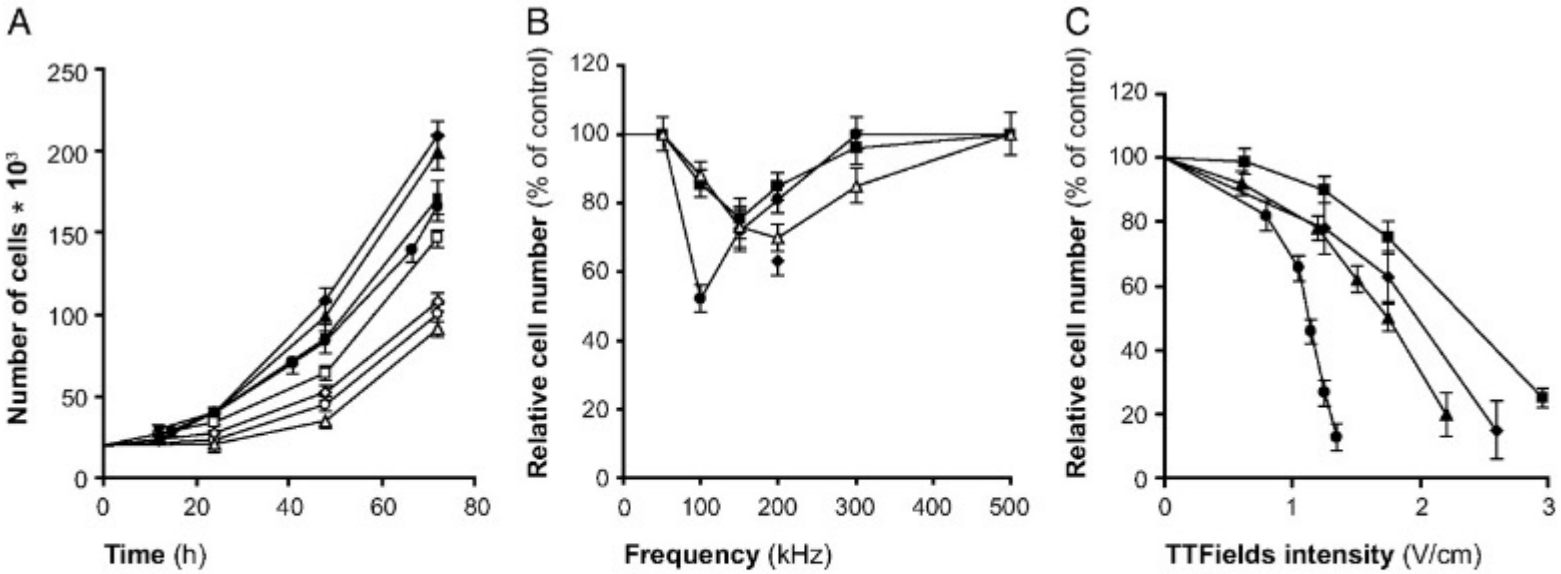


Time, frequency, and intensity dependence of the effect of TTFields on cancer cell proliferation. (A) The number of cells in untreated cultures (filled symbols) as compared with cultures treated with TTFields (open symbols) for 24 h (1.75 V/cm for MDA-MB-231, F-98, and H1299 cells and 1.1 V/cm for B16F1 cells). (B) The relative change in number of cells after 24 h of treatment of different frequencies (same TTFields intensity). (C) The effect of 24 h of exposure to TTFields of increasing intensities (at optimal frequencies). ● and ○, B16F1; ■ and □, MDA-MB-231; ▲ and △, F-98; ♦ and ◇, H1299.

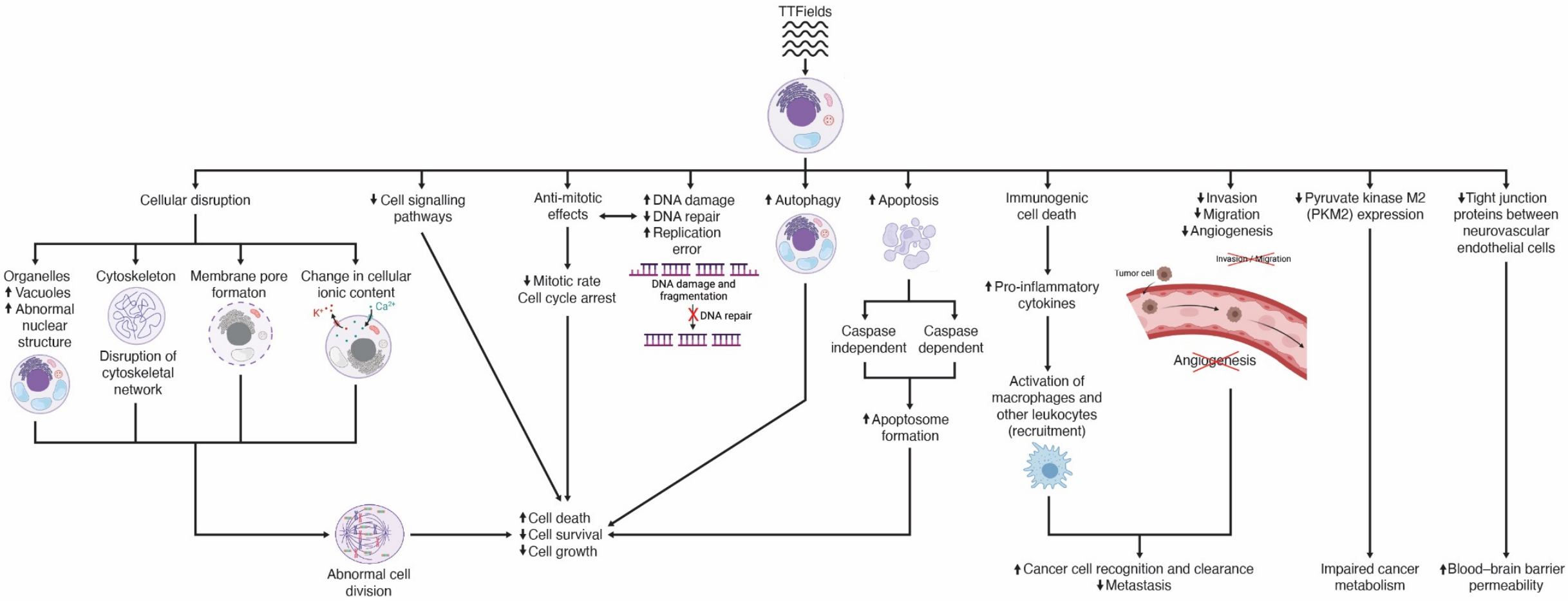
Kirson et al., 2007, PNAS

The TTFields frequency depends on the cancer cells being treated

Normal Intestine	Breast Cancer	Pancreatic Cancer	NSCLC	Ovarian Cancer	GBM	SCLC
~50 kHz	120 kHz	150 kHz	150 kHz	200 kHz	200 kHz	200 kHz

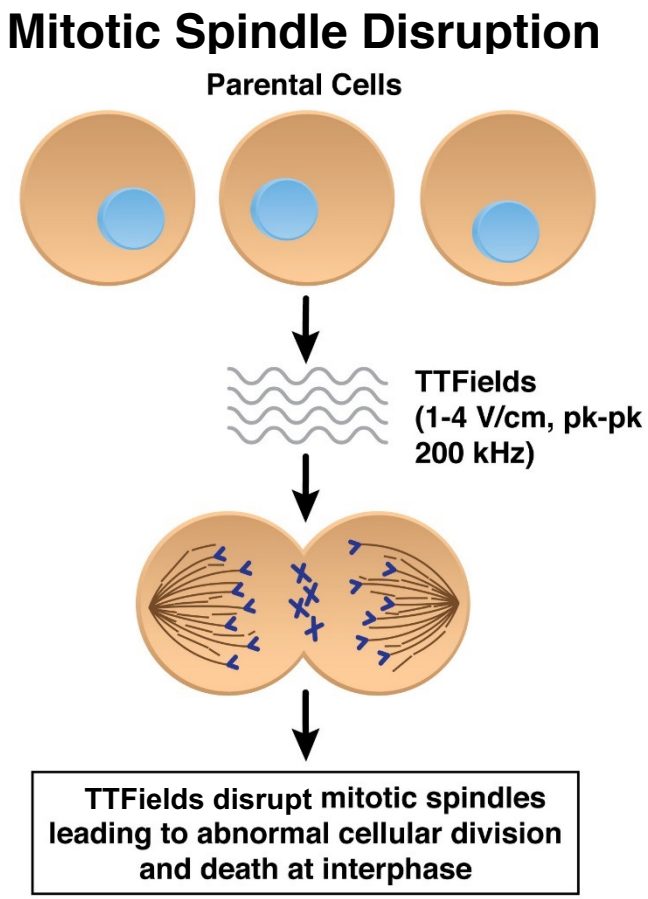
Benson, 2018

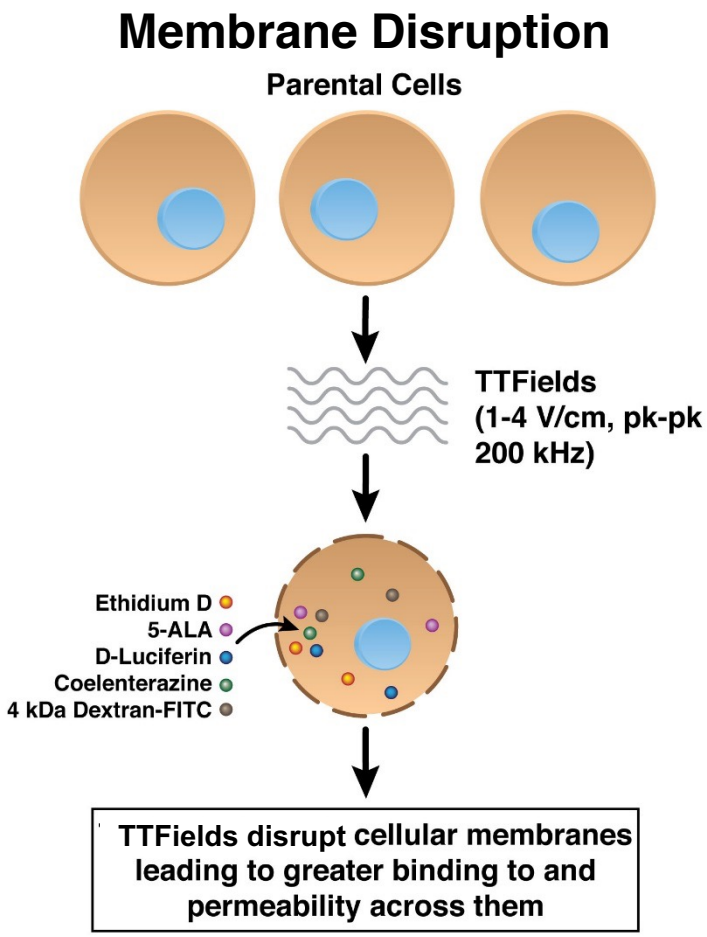
Anti-Cancer Mechanisms of TTFields



Shams and Patel, 2022, *JMCB*

Tumor Treating Fields (TTFields): Alternative Mechanism of Action





Chang*, Patel*, et al., 2018, *CDD*

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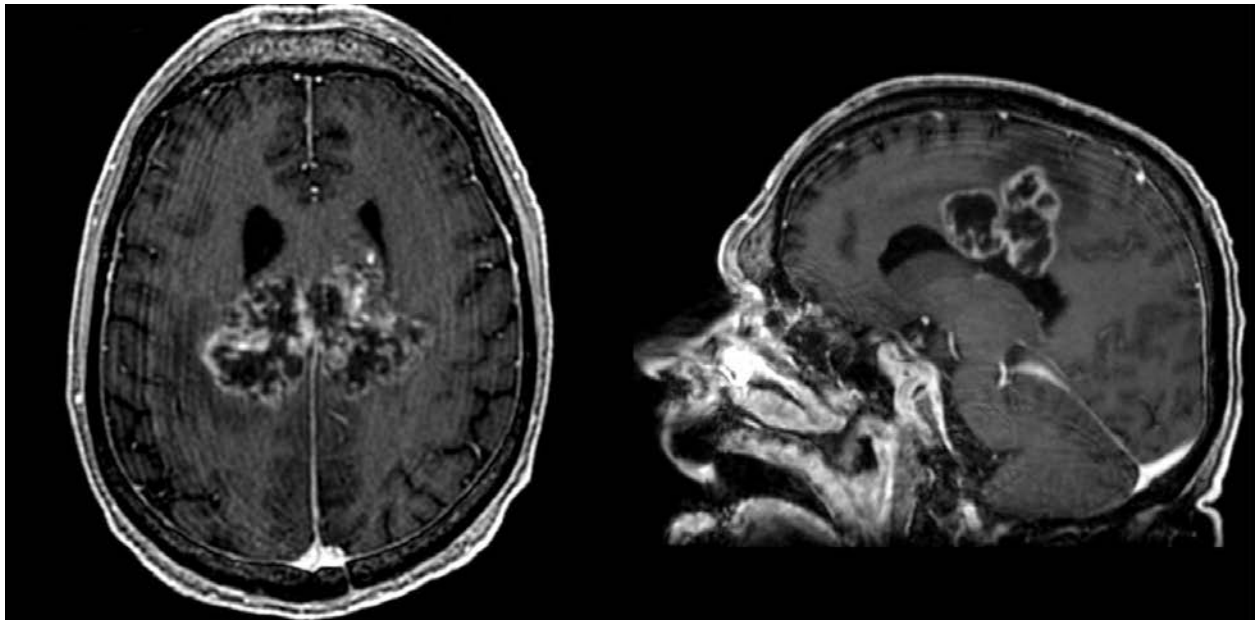
Glioblastoma (GBM)

- Most common and lethal form of primary brain cancer
  - Median overall survival: 12-16 months
  - 5-year survival: ~5%
- Standard of care: Surgery, Radiation therapy, Chemotherapy



Tumor Treating Fields (TTFields): Using Alternating Electric Fields to Treat GBM

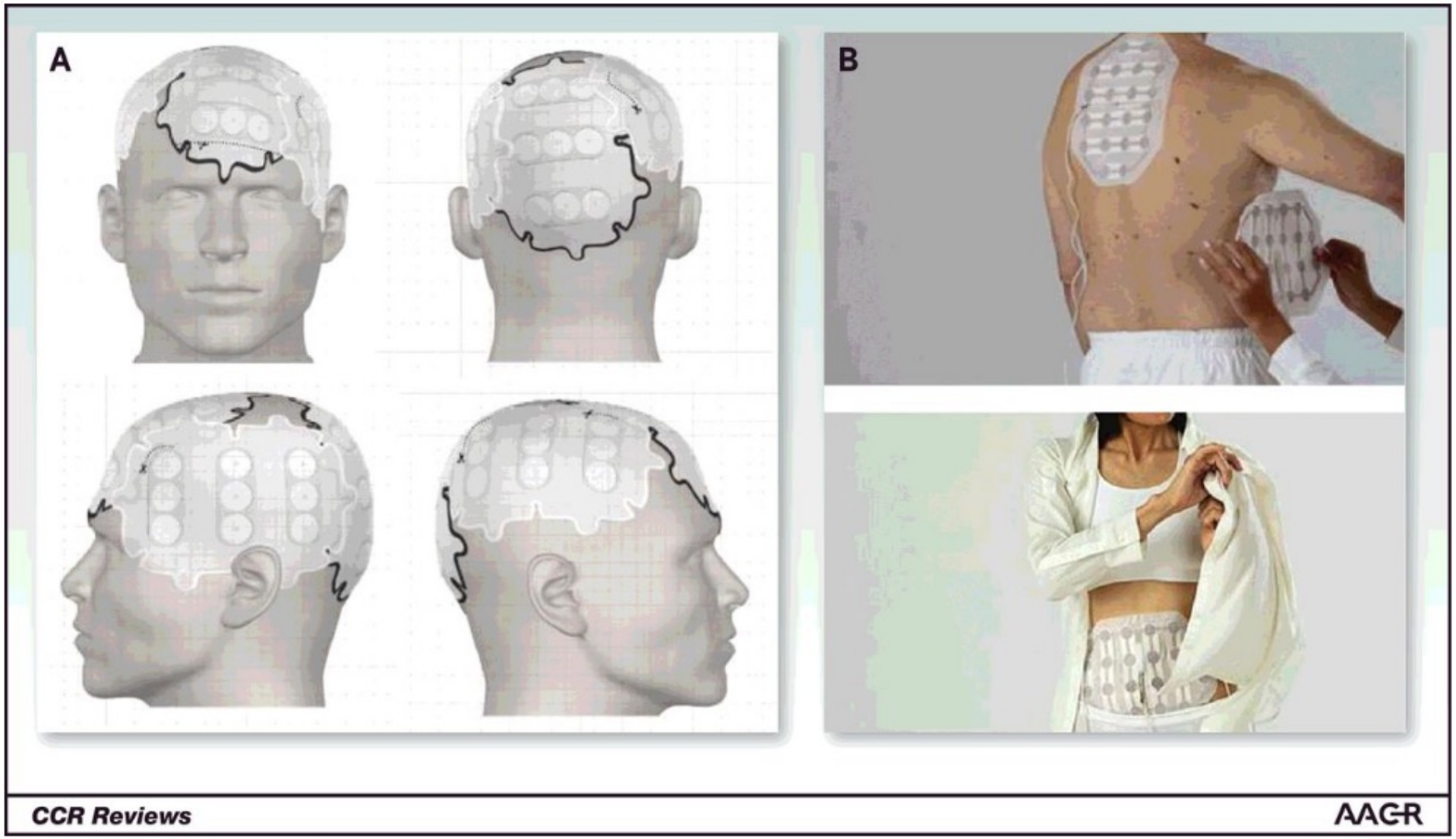
- <u>FDA Approvals</u>
  - 2011: Recurrent GBM (200 kHz)
  - 2015: Newly-diagnosed GBM (200 kHz)
  - 2016: 2nd generation GBM device
  - 2019: Malignant pleural mesothelioma (150 kHz)
- <u>National Comprehensive Cancer Network (NCCN) Guidelines</u>
  - 2018: Category 1 designation for newly-diagnosed GBM
- <u>Other positive phase 3 clinical trials (OS)</u>
  - 2023: Non-small cell lung cancer (150 kHz)

Images: Novocure, Ltd.

Wearable system for TTFields therapy in GBM

Kinzel et al, 2019

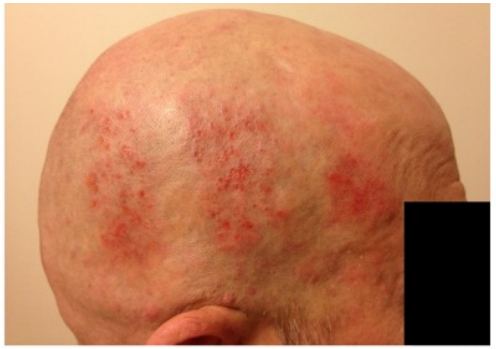
TTFields Transducer Array Placement



Mun et al, 2018

Most frequent TTFields toxicity: Skin

Contact dermatitis



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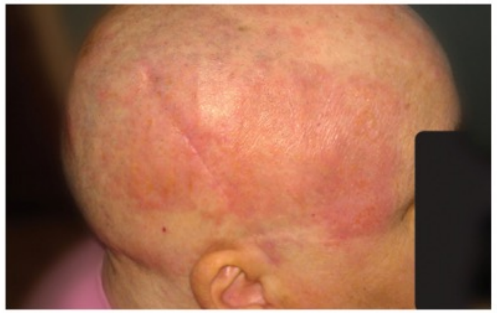


Figure 4. Contact dermatitis (may or may not be symptomatic). (A) Erythema from scalp irritation that was caused by the adhesive tapes or hydrogel. The allergic dermatitis resolved with the application of a topical corticosteroid. (60-year-old man who had been on temozolomide and NovoTTF Therapy for 7 months). (B) Irritant reaction on the right side of scalp with erythema corresponding to the three strips of hydrogel on the transducer arrays. This adverse event occurred during the hottest days in the summer and was a result of a combination of high ambient temperature, increased humidity, excessive sweating, and patient sleeping on the right side of her head. Treatment required 1-2 weeks of device interruption and use of a topical corticosteroid (65-year-old woman who had been on NovoTTF Therapy for 2 months).

Erosions & Folliculitis

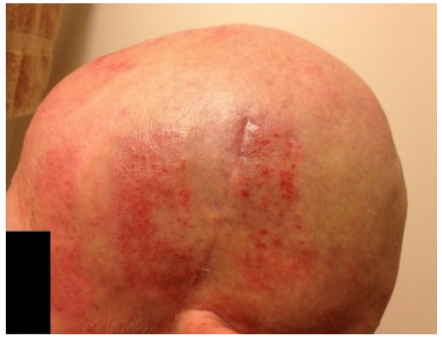
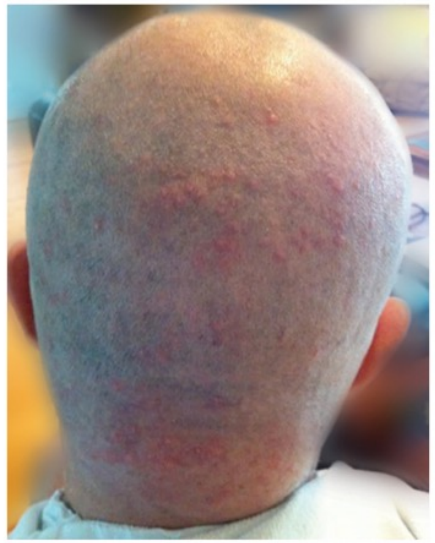


Figure 5. Dermatologic erosions and skin infectio (folliculitis) in a 60-year-old man who had been o temozolomide and NovoTTF Therapy for 3 months.

Folliculitis

A



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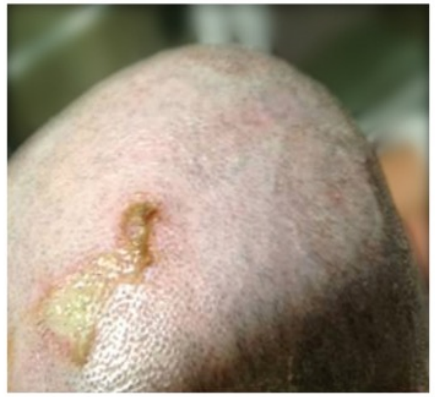


Figure 6. Skin infection/folliculitis. (A) Folliculitis (62-year-old man after receiving NovoTTF Therapy for 4 weeks). (B) Skin infection (41-year-old woman after receiving NovoTTF Therapy for 3.5 weeks).

Skin ulceration

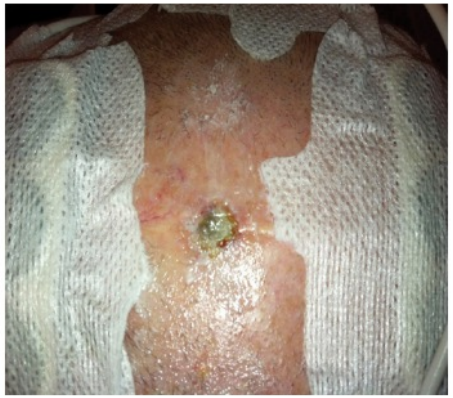


Figure 7. Skin ulceration. Note how the arrays are arranged around the site of the ulcer (61-year-old man after receiving NovoTTF Therapy for 2 weeks).

Lacouture et al, 2014

Most frequent TTFields toxicity: Skin

Figure 8. Preventive measures. Illustration of shifting transducer arrays at each array exchange.

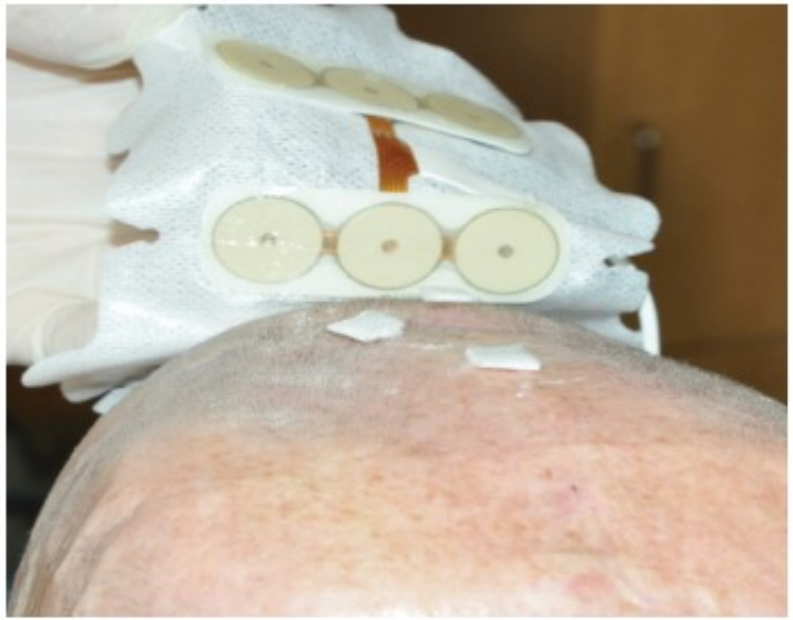
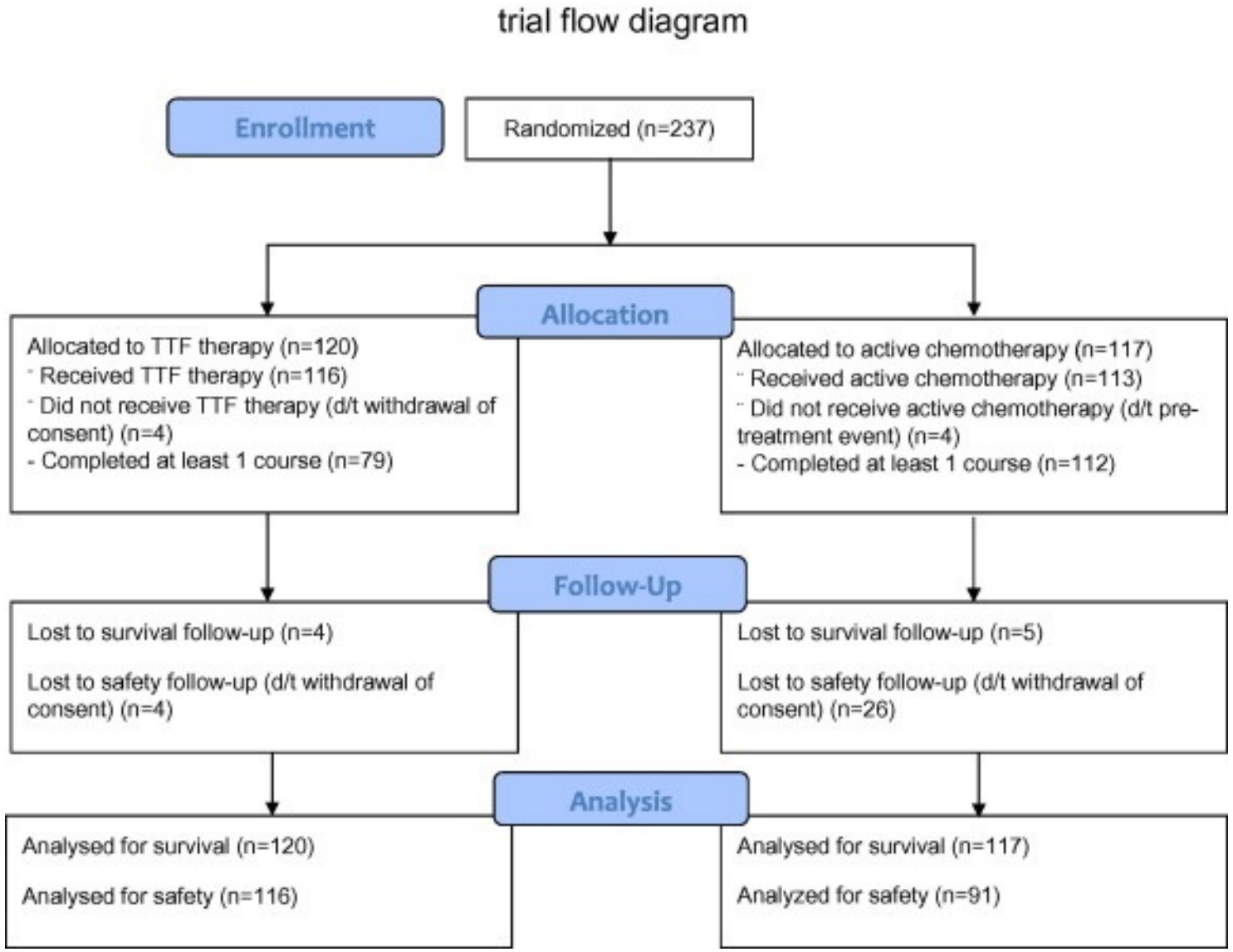


Figure 9. Example of protection of sites of dermatologic adverse events with small sterile nonstick gauze barriers. (Note: gauze should not be directly beneath any of the array ceramic disks.)

Lacouture et al, 2014

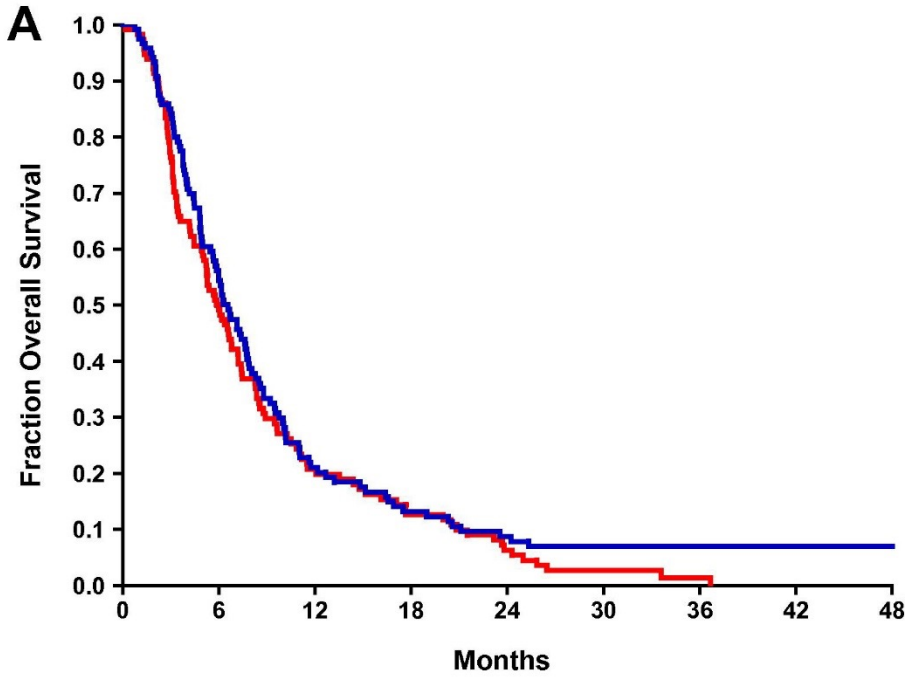
First TTField device FDA Approval in 2011 based on EF-11 phase 3 trial in recurrent GBM (rGBM)



Stupp et al, 2012

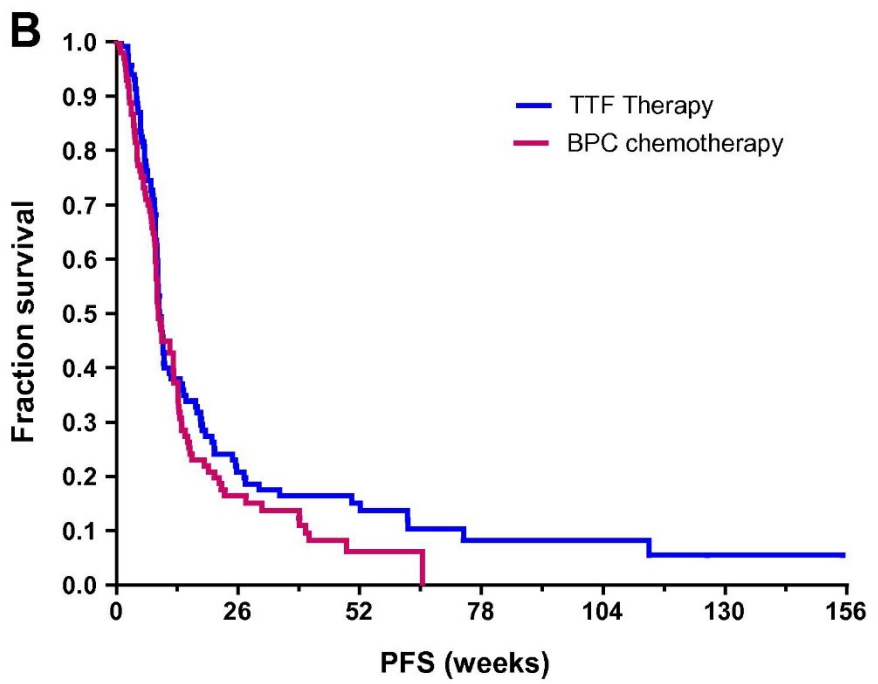
Survival Analysis of EF-11 trial: TTFields alone is non-inferior to chemo alone

Overall Survival (OS)



At risk	0 m	6 m	12 m	18 m	24 m	30 m	36 m	42 m	48 m
TTF	120	63	24	15	9	7	4	2	1
BPC	117	56	22	14	6	2	1	0	0

Progression-Free Survival (PFS)



0 m	13 w	26w	39w	52w	65 w	78 w	91 w
120	38	19	14	11	6	4	3
117	34	14	10	3	1	0	0

Stupp et al, 2012

Side Effects / Toxicity in EF-11 trial

Due to TTFields alone (Grade 1/2 toxicities)

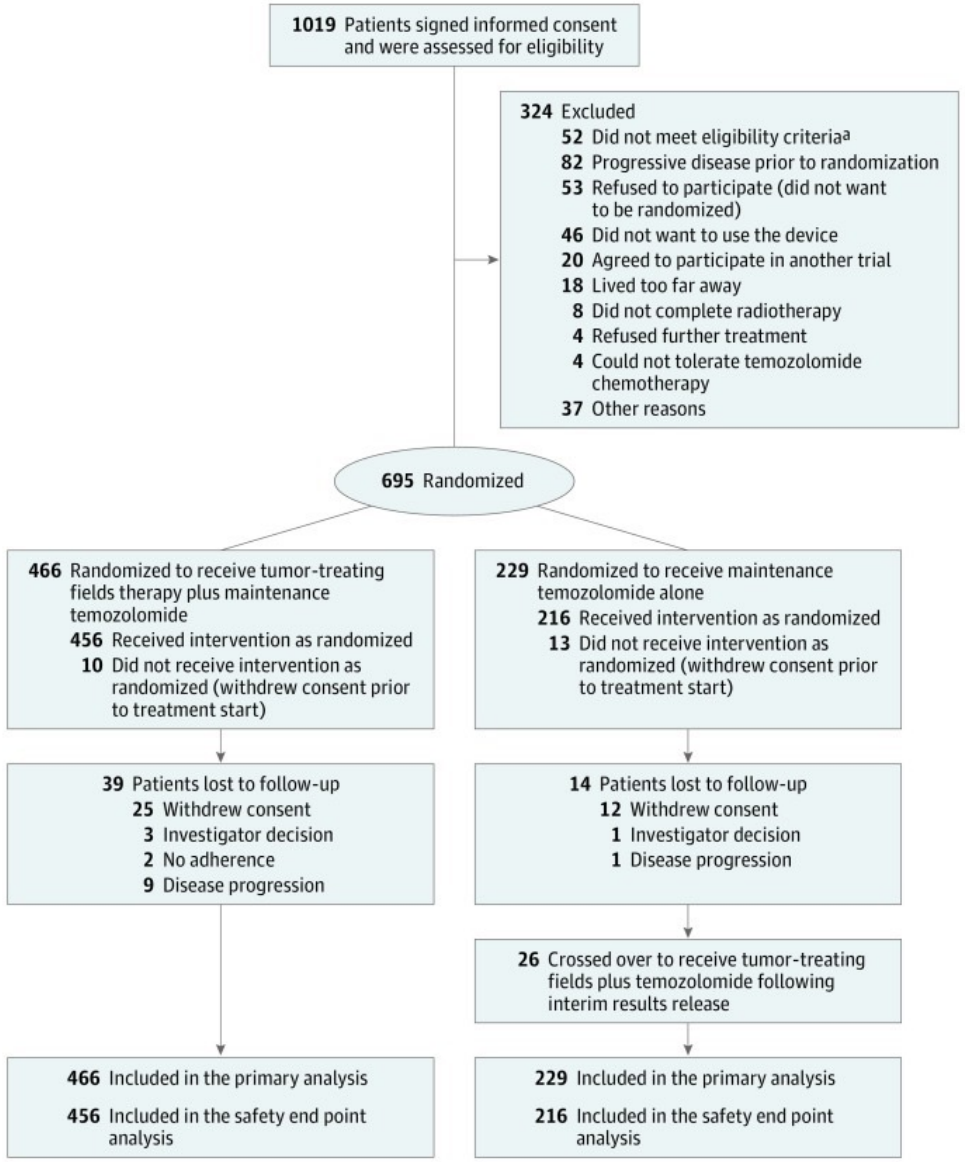
- 16% mild-to-moderate contact dermatitis on the scalp below the transducer arrays. Managed with steroid creams

Due to chemotherapy alone (Grade 3/4 toxicities)

- 4% hematological (1% for TTFields)
- 3% gastrointestinal (<1% for TTFields)
- 2% seizures (2% for TTFields)
- <1% headaches (1% for TTFields)
- 3% vascular disorders (1% for TTFields)

Stupp et al, 2012

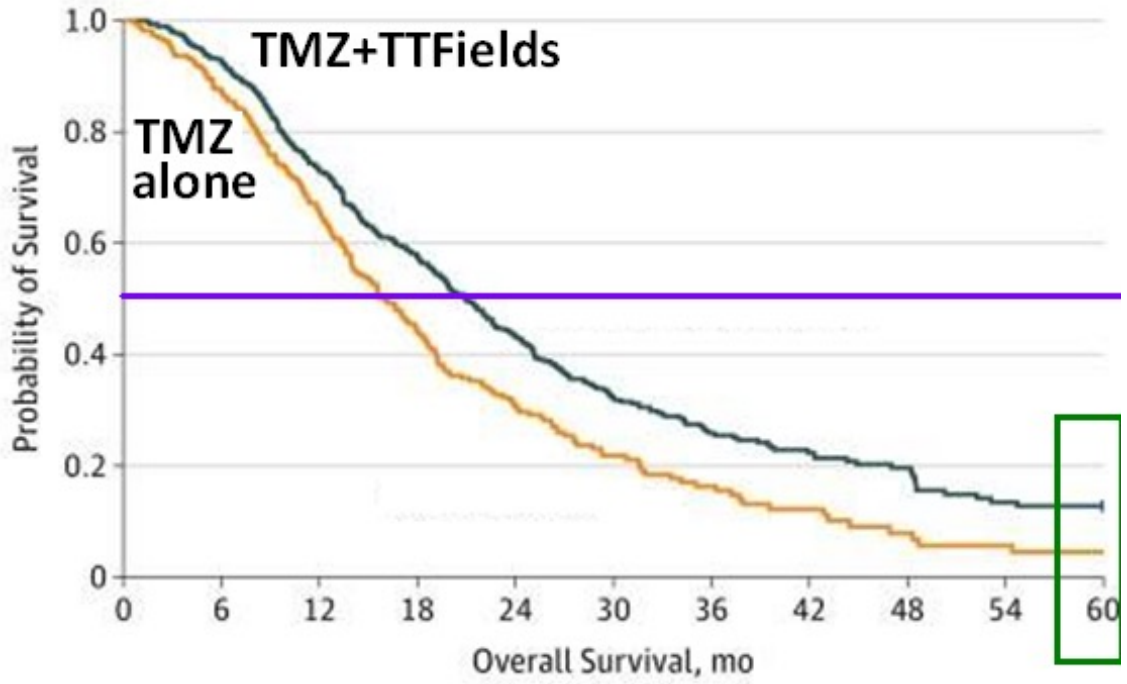
Second TTFields Device FDA Approval in 2015 based on EF-14 phase 3 trial in newly-dx GBM (nGBM)



Stupp et al, 2017

TTFields+Monthly TMZ in EF-14 trial

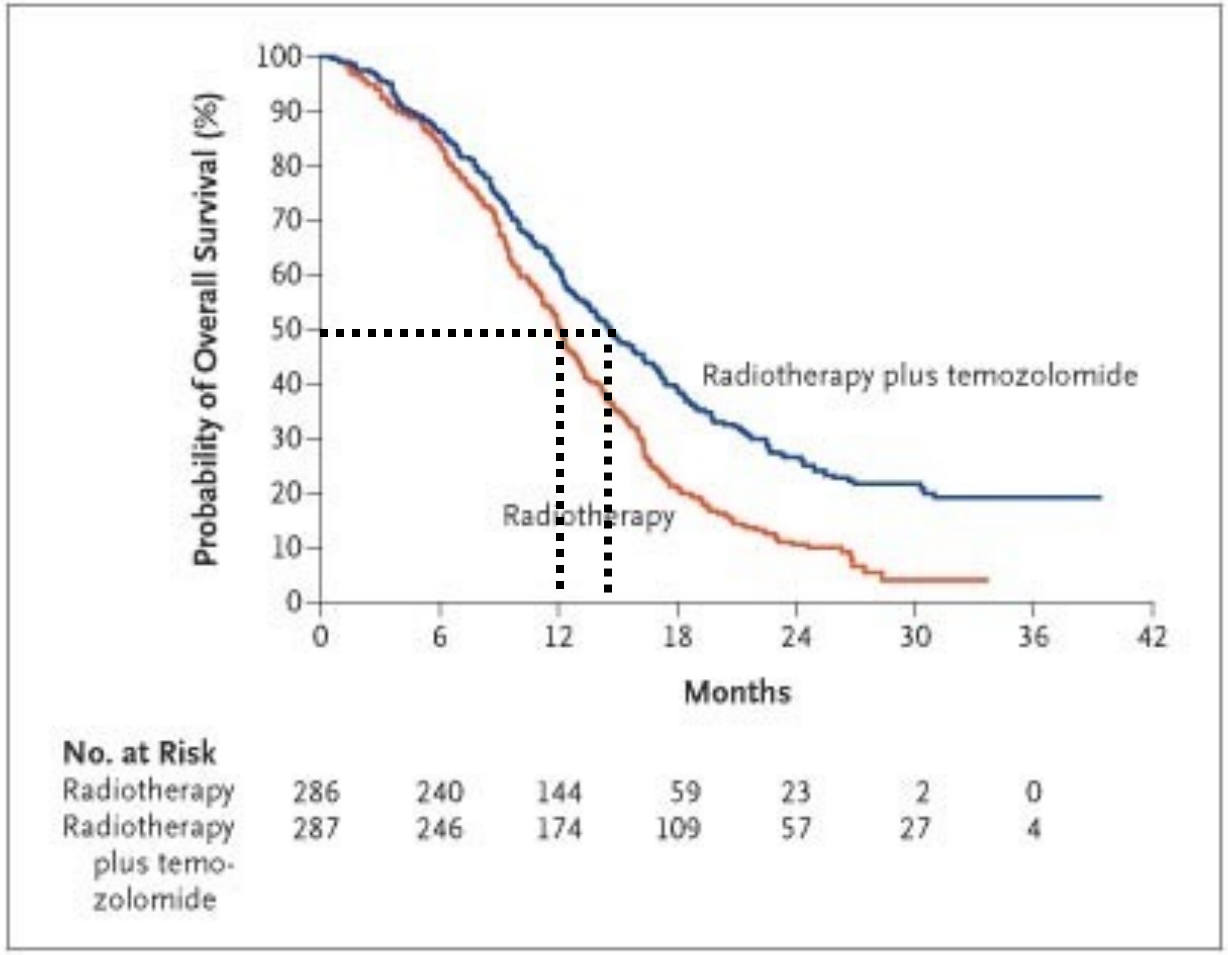
	TMZ alone	TMZ + TTFields
Median overall survival in months (95% CI)	16.0 (14.0 - 18.4)	20.9 (19.3 - 22.7)
5-year survival rate as a percent (95% CI)	5% (2%-11%)	13% (9%-18%)



- Standard of care for GBM includes surgical resection, then concurrent radiation and chemotherapy (TMZ), followed by maintenance TMZ
- TTFields added to maintenance TMZ prolongs overall survival in GBM patients

Stupp et al, 2017

Reminder: Survival Benefit of temozolomide (TMZ) chemotherapy



<u>Median Overall Survival (mOS)</u>

- Radiation alone: 12.1 months
- Radiation + TMZ: 14.6 months

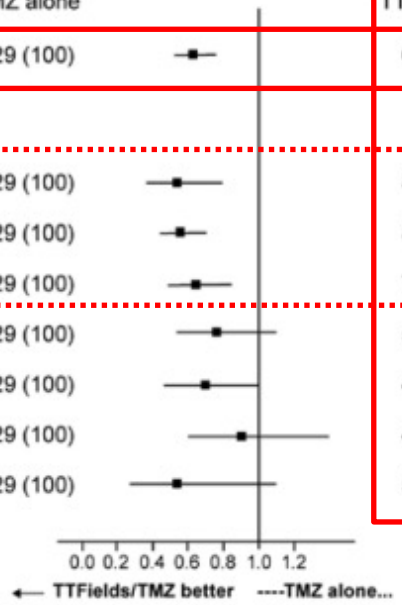
Difference in mOS: 2.5 months

Stupp et al, 2005

(EF-14) Increased compliance with 200 kHz TTFields is prognostic for improved survival in the treatment of GBM: a subgroup analysis

Progression-Free Survival

Subgroup	No. of patients (%)		Hazard ratio	Median PFS (months)	
	TTFields/TMZ	TMZ alone		TTFields/TMZ	TMZ alone
Overall	450 (100)	229 (100)		6.7	4
TTFields compliance					
>90	43 (10)	229 (100)		8.2	4
80–90	166 (37)	229 (100)		8.1	4
70–80	91 (20)	229 (100)		7.7	4
60–70	46 (10)	229 (100)		5.4	4
50–60	42 (9)	229 (100)		4.2	4
30–50	40 (9)	229 (100)		4.8	4
≤30	22 (5)	229 (100)		5.9	4



Overall Survival

Subgroup	No. of patients (%)		Hazard ratio	Median OS (months)	
	TTFields/TMZ	TMZ alone		TTFields/TMZ	TMZ alone
Overall	450 (100)	229 (100)		20.9	16
TTFields compliance					
>90	43 (10)	229 (100)		24.9	16
80–90	166 (37)	229 (100)		21.5	16
70–80	91 (20)	229 (100)		21.7	16
60–70	46 (10)	229 (100)		19.9	16
50–60	42 (9)	229 (100)		18	16
30–50	40 (9)	229 (100)		17.9	16
≤30	22 (5)	229 (100)		18.2	16

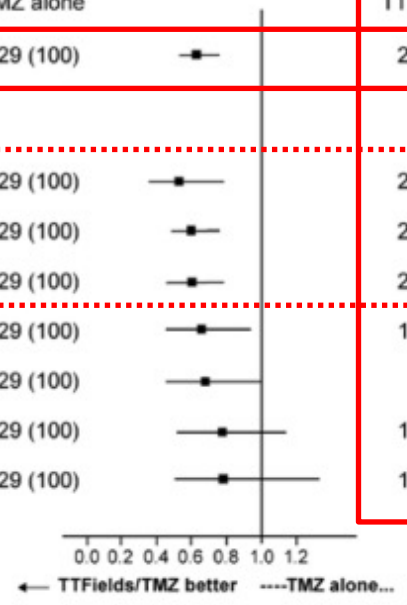


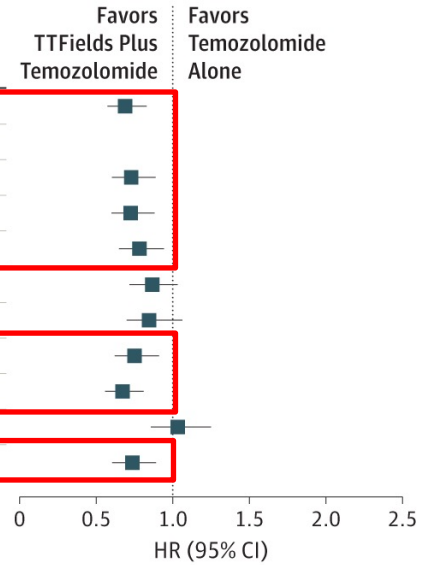
Fig. 1 Forest plots show the effect of treatment compliance with TTFields plus TMZ on PFS and OS. A threshold value of 50% compliance with TTFields plus TMZ was needed to show a significant extension of OS compared to TMZ alone. Both PFS and OS were extended with treatment compliance levels >50%. A trend in favor of longer PFS and OS was seen with higher rates of treatment compliance

Toms et al, 2019

(EF-14) Influence of 200 kHz TTFields treatment on Health-Related Quality of Life of Patients With Newly Diagnosed GBM: A 2º Analysis

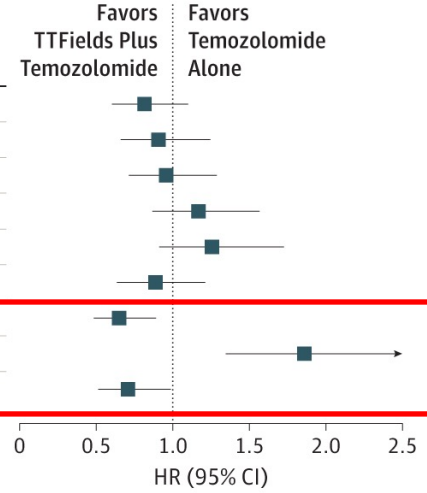
A Deterioration-free survival

Source	Median, mo: TTFields Plus Temozolomide	Median, mo: Temozolomide Alone	HR (95% CI)
Progression-free survival	6.7	4.0	0.69 (0.57-0.83)
Deterioration-free survival			
Global health status	4.8	3.3	0.73 (0.60-0.88)
Physical functioning	5.1	3.7	0.73 (0.60-0.88)
Cognitive functioning	4.4	3.6	0.78 (0.64-0.94)
Role functioning	4.3	3.8	0.86 (0.71-1.02)
Social functioning	4.5	3.9	0.84 (0.70-1.06)
Emotional functioning	5.3	3.9	0.75 (0.62-0.91)
Pain	5.6	3.6	0.67 (0.56-0.81)
Itchy skin	3.9	4.0	1.03 (0.85-1.25)
Weakness of legs	5.6	3.9	0.74 (0.61-0.89)



B Time to deterioration

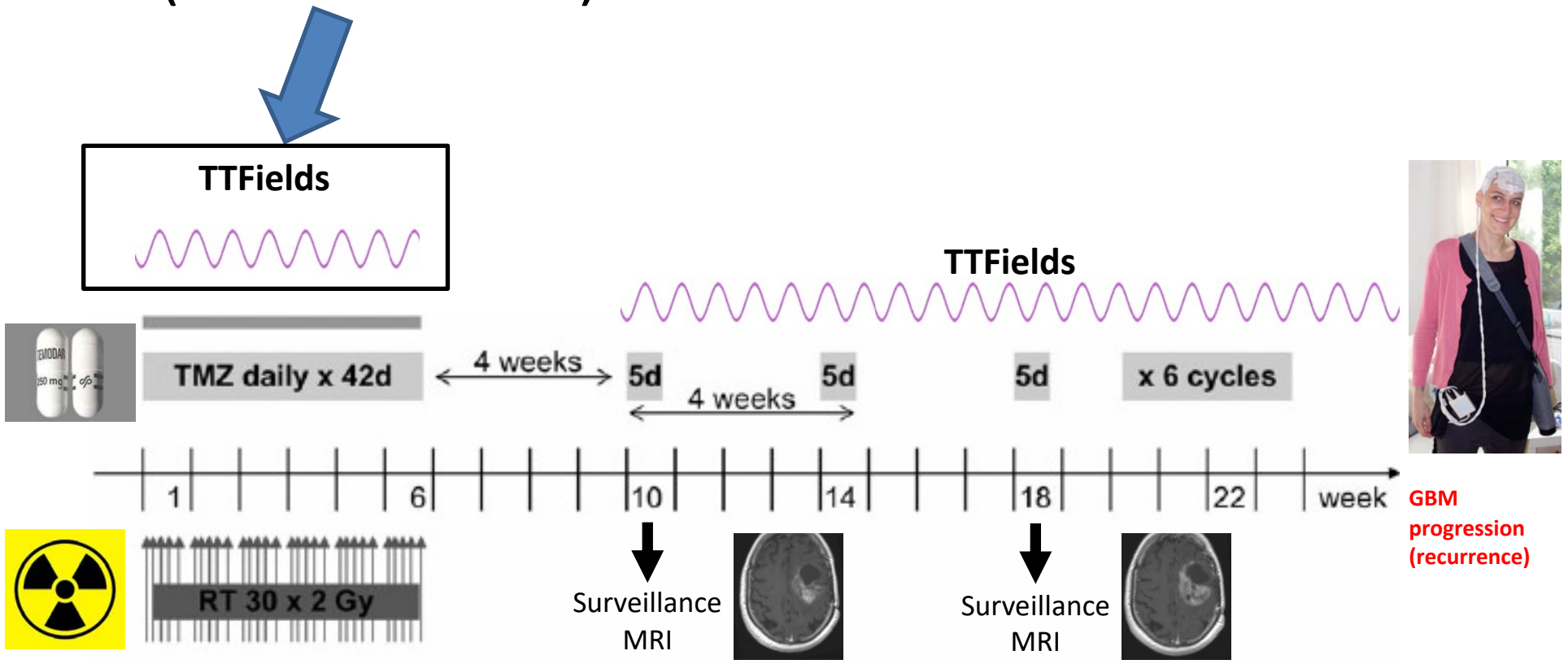
Source	Median, mo: TTFields Plus Temozolomide	Median, mo: Temozolomide Alone	HR (95% CI)
Global health status	14.130	9.63	0.81 (0.60-1.10)
Physical functioning	14.170	13.97	0.90 (0.66-1.24)
Cognitive functioning	10.270	13.97	0.95 (0.71-1.28)
Role functioning	9.20	13.97	1.16 (0.86-1.56)
Social functioning	10.60	13.97	1.25 (0.91-1.72)
Emotional functioning	13.430	14.03	0.88 (0.64-1.21)
Pain	13.370	12.13	0.65 (0.48-0.89)
Itchy skin	8.167	14.40	1.85 (1.33-2.57)
Weakness of legs	14.170	14.03	0.71 (0.51-0.99)



Taphoorn et al, 2018

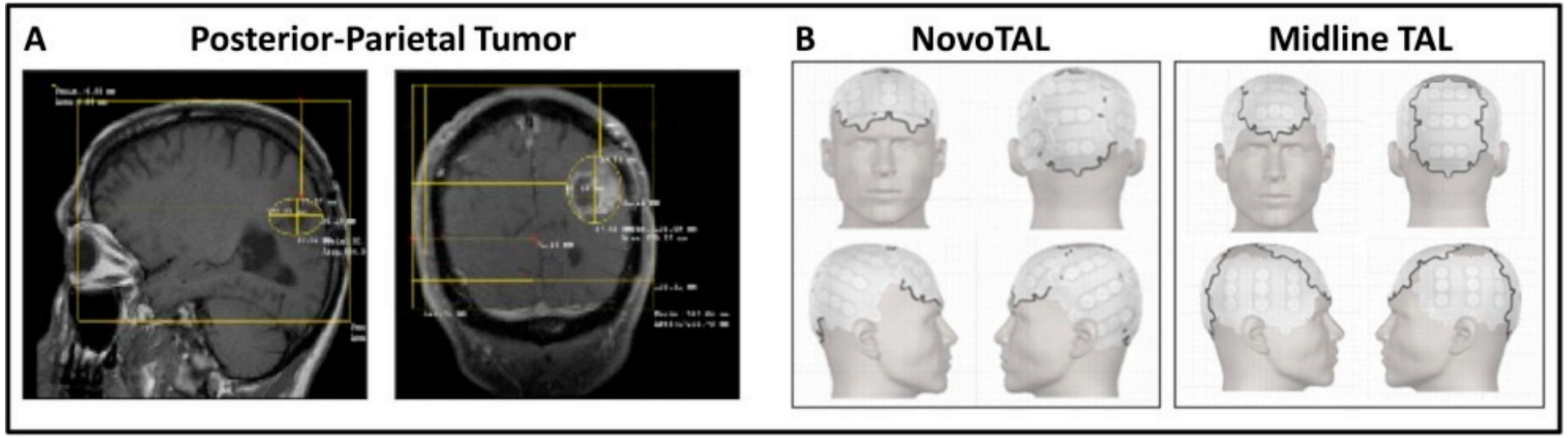
Third clinical trial of TTField device underway in nGBM patients

- (EF-32) 200 kHz TTFields + radiation + TMZ chemotherapy in newly-diagnosed GBM (NCT04471844) “TRI-dent” trial



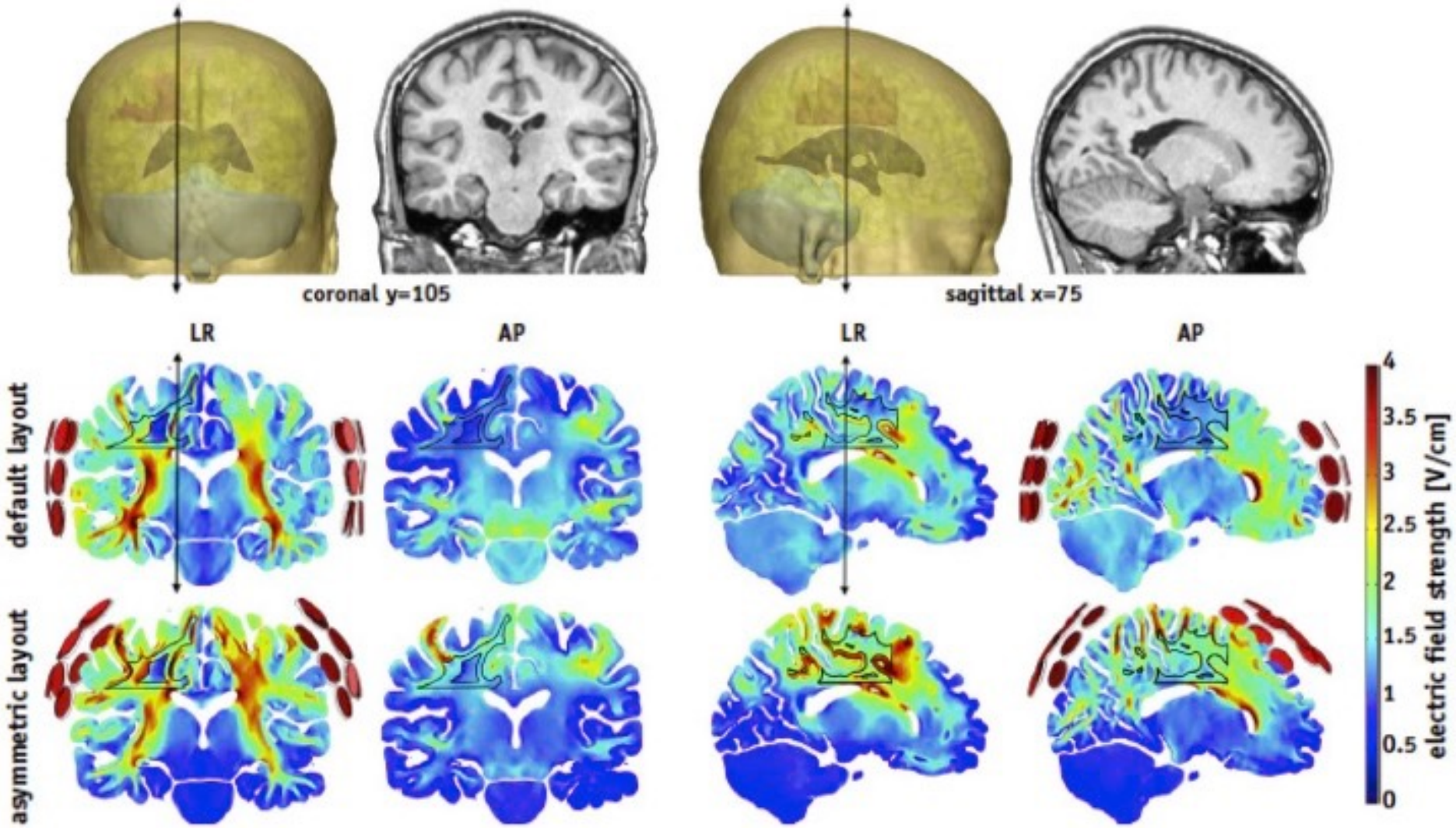
Planning TTField Device Therapy

- Certified prescribers in neuro-oncology: Drs. Puduvalli, Kamiya, and Patel
- Individualized treatment mapping (can be done by the certified prescriber, or the patient's brain MRI CD can be sent to the manufacturer for mapping to be done there)



Benson, 2018

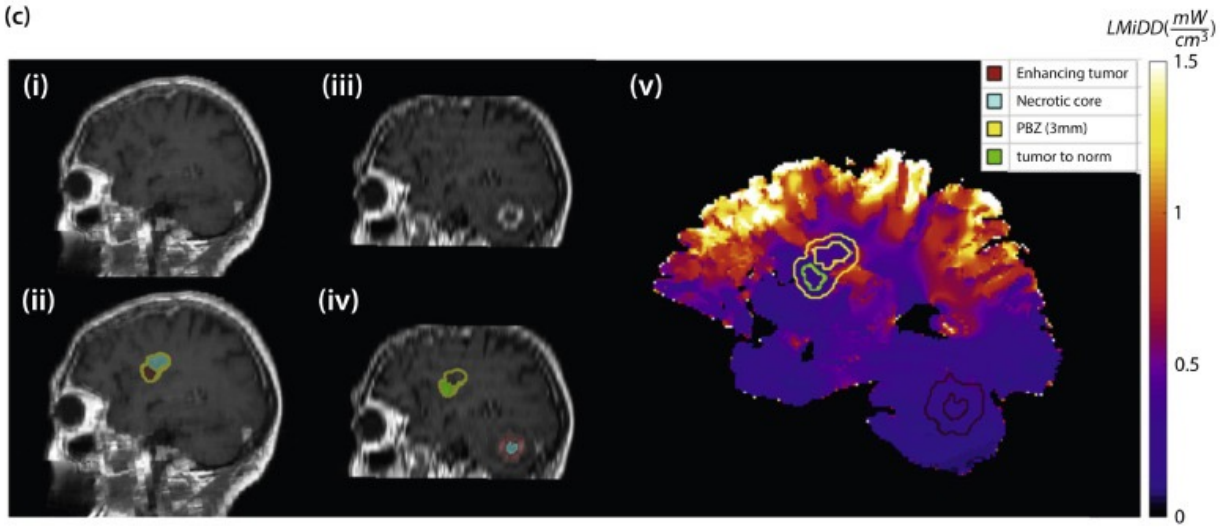
Planning TTField Device Therapy



Benson, 2018

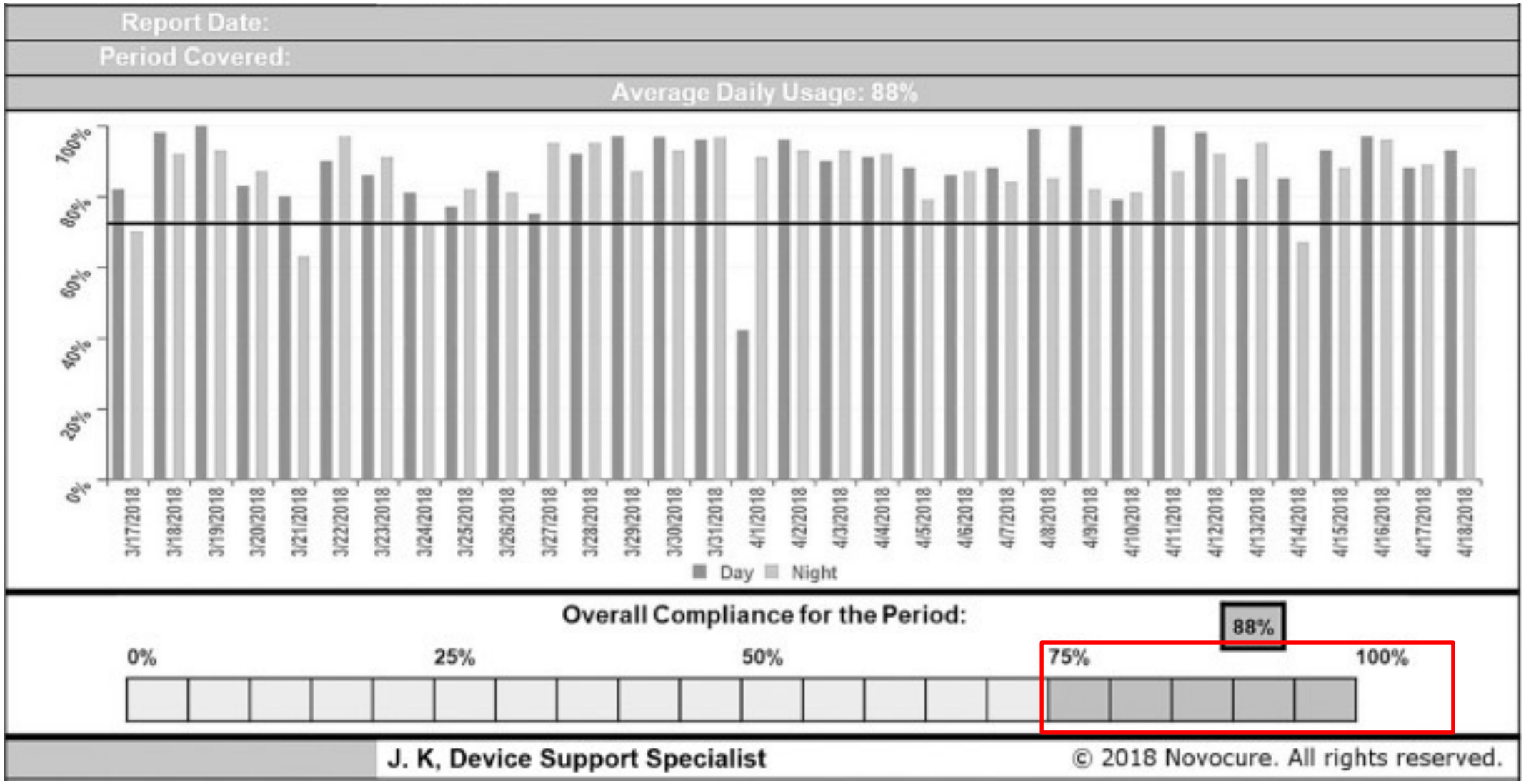
What is the “dose” of TTFields?

- It is the product of the time “on” and the square of the electric field strength that reaches the tumor: t × E^2
- Recommended “on time” is 75% of the time, averaged over a month. Approximately 18 hours/day



Glas et al, 2022

TTField device patient usage reports



Anthony et al, 2018

Agenda

Tumor Treating Fields

MODULE 1: Tumor Treating Fields with Dr Chirag Patel

- Mechanism of action of tumor treating fields
- Tumor treating fields in glioblastoma multiforme
- Tumor treating fields in other tumor types
- Case presentations

PARP Inhibitor Therapy in Ovarian Cancer

MODULE 2: Updates on PARP Inhibitors in 2023 with Dr Gottfried Konecny

- PARP inhibitors as up-front maintenance therapy for ovarian cancer
- PARP inhibitors for recurrent ovarian cancer

Tumour Treating Fields in combination with pemetrexed and cisplatin or carboplatin as first-line treatment for unresectable malignant pleural mesothelioma (STELLAR): a multicentre, single-arm phase 2 trial

FDA approval based on single-arm study results compared to historical control:

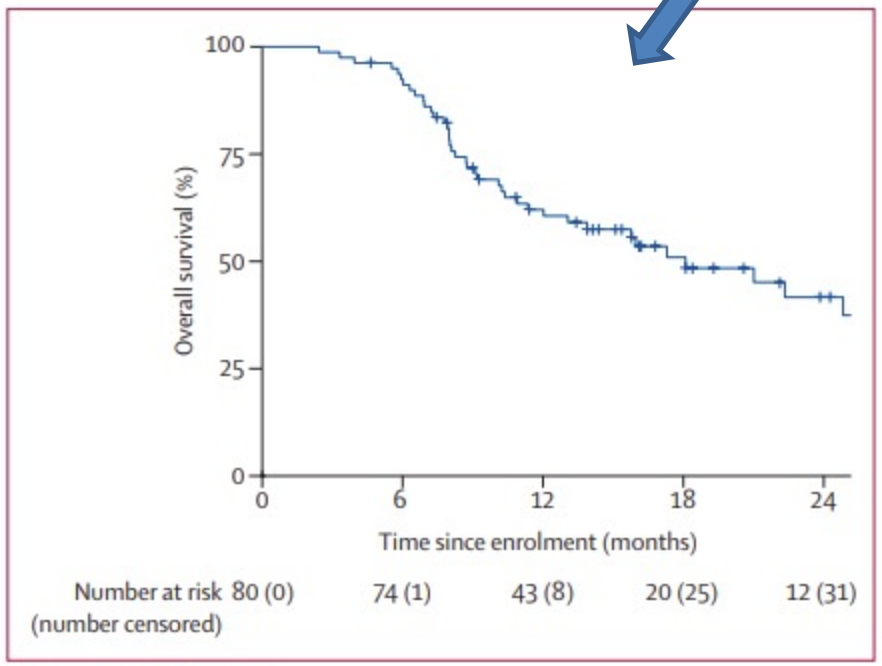
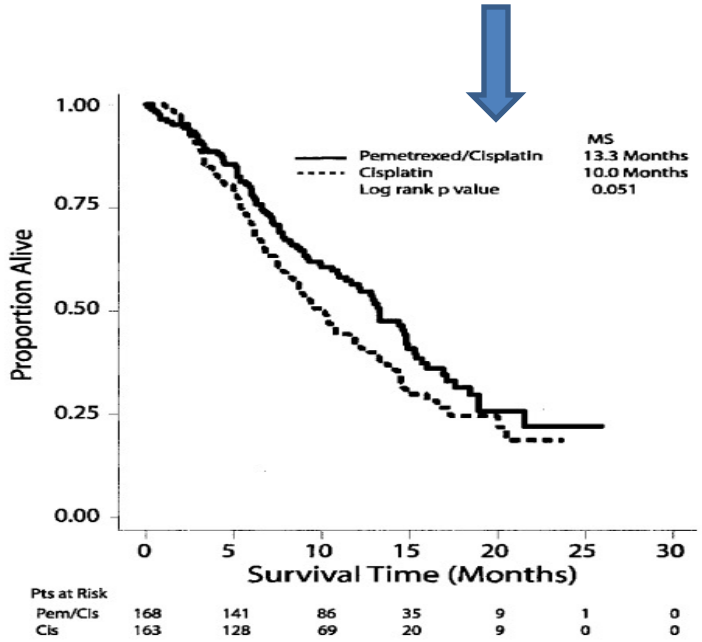


Figure 2: **Overall survival**
Kaplan-Meier analyses of overall survival in the intention-to-treat population.



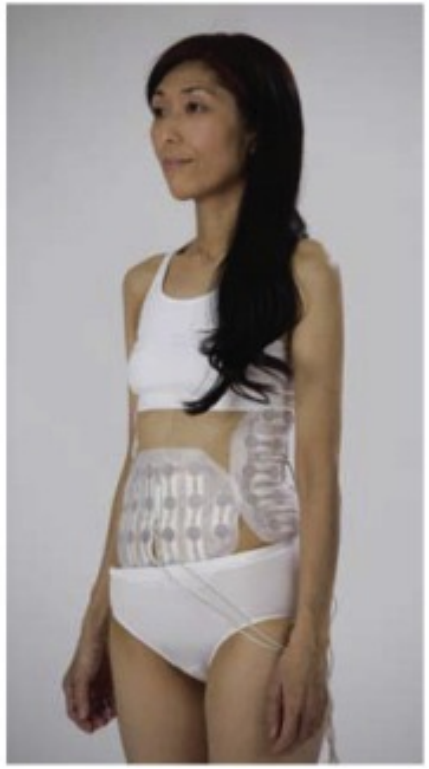
150 kHz TTFields for ≥18 hrs/day +
(cisplatin or carboplatin) + pemetrexed
mOS: 18.2 months (95% CI 12.1–25.8)
Ceresoli et al., 2019, *Lancet Oncol*

cisplatin + pemetrexed

mOS: 13.3 months
Vogelzang et al., 2003, *JCO*

Tumor Treating Fields in combination with paclitaxel in recurrent ovarian carcinoma: Results of the INNOVATE pilot study

- Phase 2, single-arm clinical trial
- 200 kHz TTFields + weekly paclitaxel for 8 weeks
- N=31 patients with recurrent, platinum resistant ovarian carcinoma



Vergote et al., 2018, *Gyn Oncol*

Tumor Treating Fields in combination with paclitaxel in recurrent ovarian carcinoma: Results of the INNOVATE pilot study

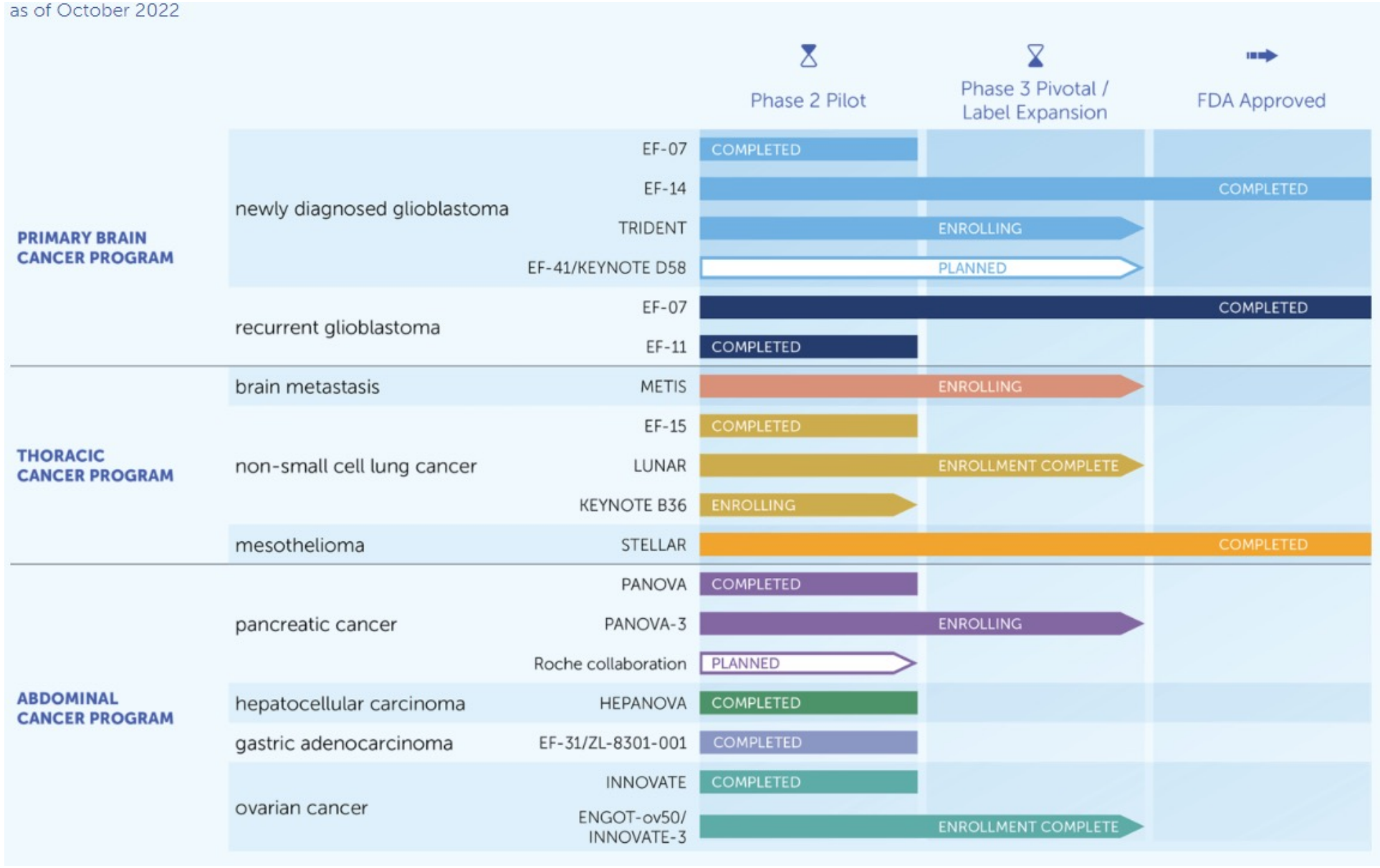
Table 3
Clinical outcomes reported on the INNOVATE Study.

Clinical outcome	TTFields + paclitaxel ($n = 31$)
Overall survival	
Median overall survival mo (95% CI)	Not reached
Survival rate, % (95% CI)	
At 6 months	90 (72–97)
At 12 months	61 (37–78)
Progression free survival	
Median progression free survival mo (95% CI)	8.9 (4.7-NA)
Progression free survival rate, % (95% CI)	
At 6 months	57 (37–72)
Best response per RECIST Criteria V1.1 in patients with available radiological data, no. (%)	28 (90)
Complete response	0 (0)
Partial response	7 (25)
Stable disease	13 (46)
Progressive disease	8 (29)
Clinical benefit (combining stable disease and partial response), no. (%)	20 (71)

- Conclusion. TTFields combined with weekly paclitaxel were safe in platinum-resistant recurrent ovarian cancer and warrant evaluation in a randomized phase 3 trial.

Vergote et al., 2018, *Gyn Oncol*

TTFields Pipeline



Novocure, Ltd.

Future Directions

- Validating molecular and transcriptomic mechanisms in tissue samples from TTFields clinical trials
- Computational modeling
- Examining indirect effects of TTFields on cancer proliferation
  - permeabilizing blood vessels and cancer cell membranes
  - altering tumor metabolism
  - application of multiple TTFields frequencies for a single cancer
  - expanding application to spine and other tumors

Tumor Treating Fields (TTFields) Therapy plus XELOX Chemotherapy for Front Line Treatment of Advanced Unresectable Gastroesophageal Junction Adenocarcinoma (GEJC) or Gastric Adenocarcinoma (GC): A Multicenter Phase II Trial

Li J et al.

ESMO Asia 2022;Abstract LBA3.

Pivotal LUNAR Study in Non-Small Cell Lung Cancer Met Primary Overall Survival Endpoint

Press Release: January 5, 2023

"The LUNAR study met its primary endpoint, demonstrating a statistically significant and clinically meaningful improvement in overall survival over standard therapies alone. The LUNAR study is a pivotal, open-label, randomized study evaluating the safety and efficacy of Tumor Treating Fields (TTFields) together with standard therapies for stage 4 non-small cell lung cancer (NSCLC) following progression while on or after treatment with platinum-based therapy.

The LUNAR study also showed a statistically significant and clinically meaningful improvement in overall survival when patients were treated with TTFields and immune checkpoint inhibitors (ICI), as compared to those treated with immune checkpoint inhibitors alone, and a positive trend in overall survival when patients were treated with TTFields and docetaxel versus docetaxel alone. Patient enrollment was well balanced between the ICI and docetaxel cohorts of the experimental and control arms, and control arms performed in line with prior studies. TTFields therapy was well tolerated by patients enrolled in the experimental arm of the study."

https://www.novocure.com/novocure-announces-pivotal-lunar-study-in-non-small-cell-lung-cancer-met-primary-overall-survival-endpoint/

RTP RESEARCH TO PRACTICE

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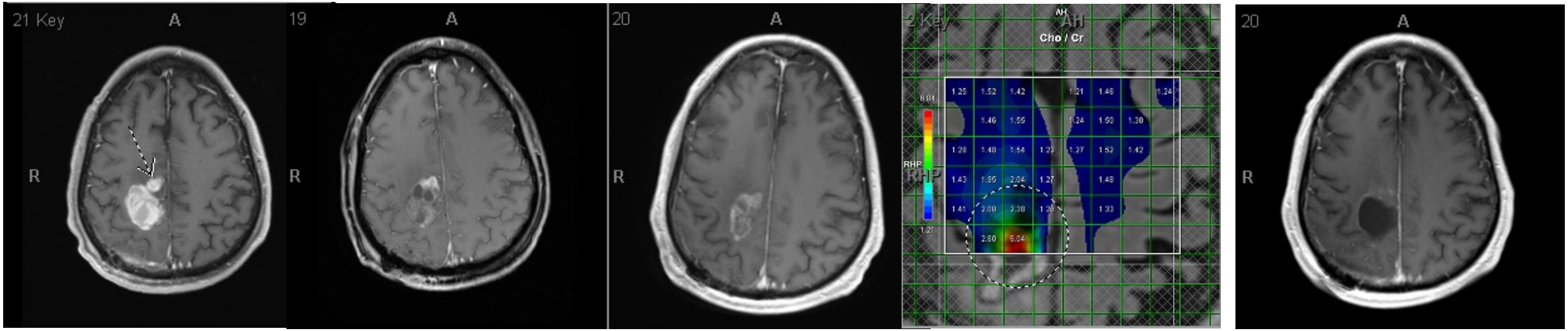
Dr Patel: Case 1

- 58 y.o. man with glioblastoma, IDH wild-type s/p biopsy at outside hospital May 2022, sub-total resection at a different outside hospital 1 month later, followed by concurrent chemoradiation with temozolomide (TMZ).
- After 2 adjuvant cycles of TMZ + 200 kHz TTFields, surveillance brain MRI showed early signs of disease progression based on advanced perfusion sequences and MR spectroscopy. TTField device usage was greater than 90%.
- Enrolled in a clinical trial of neoadjuvant immune checkpoint inhibitor followed by re-resection followed by adjuvant immune checkpoint inhibitor.



Post-op, pre-chemoradiation

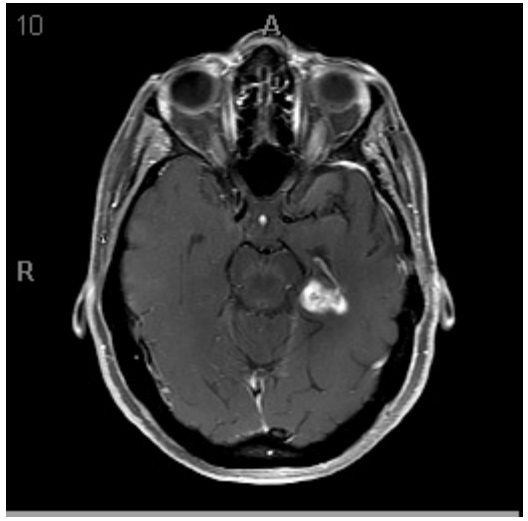
Post-chemoradiation

After 2 months on adjuvant chemo and 200 kHz TTFields: early signs of progression

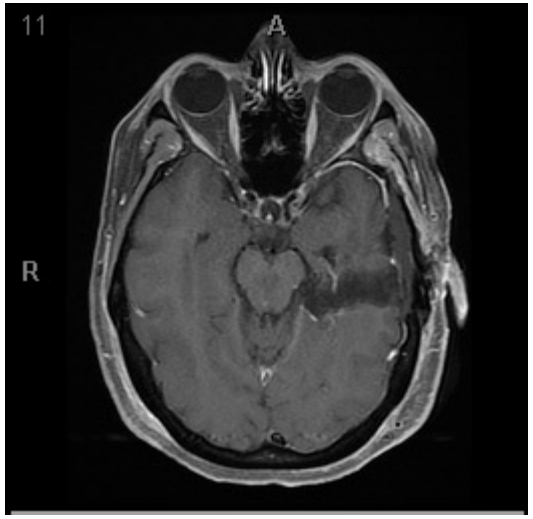
Post-op

Dr Patel: Case 2

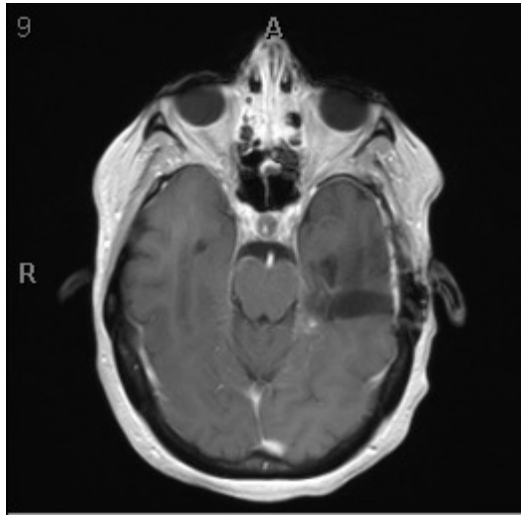
- 56 y.o. woman with left temporal glioblastoma, IDH wild-type, MGMT promoter-methylated
- s/p resection, concurrent chemoradiation with temozolomide (TMZ)
- Enrolled in AGILE trial (randomized to arm with oral paxalisib [small molecule PI3K/mTOR inhibitor] for 13 months
- Found to have progression in left temporal lobe on surveillance MRI
- Re-resection
- Re-irradiation to residual disease + bevacizumab (5 mg/kg every 2 weeks)
- Monthly adjuvant TMZ + 200 kHz TTFields device



Pre-re-resection
(time of recurrence)



Post-re-resection



Post-re-irradiation +
bevacizumab

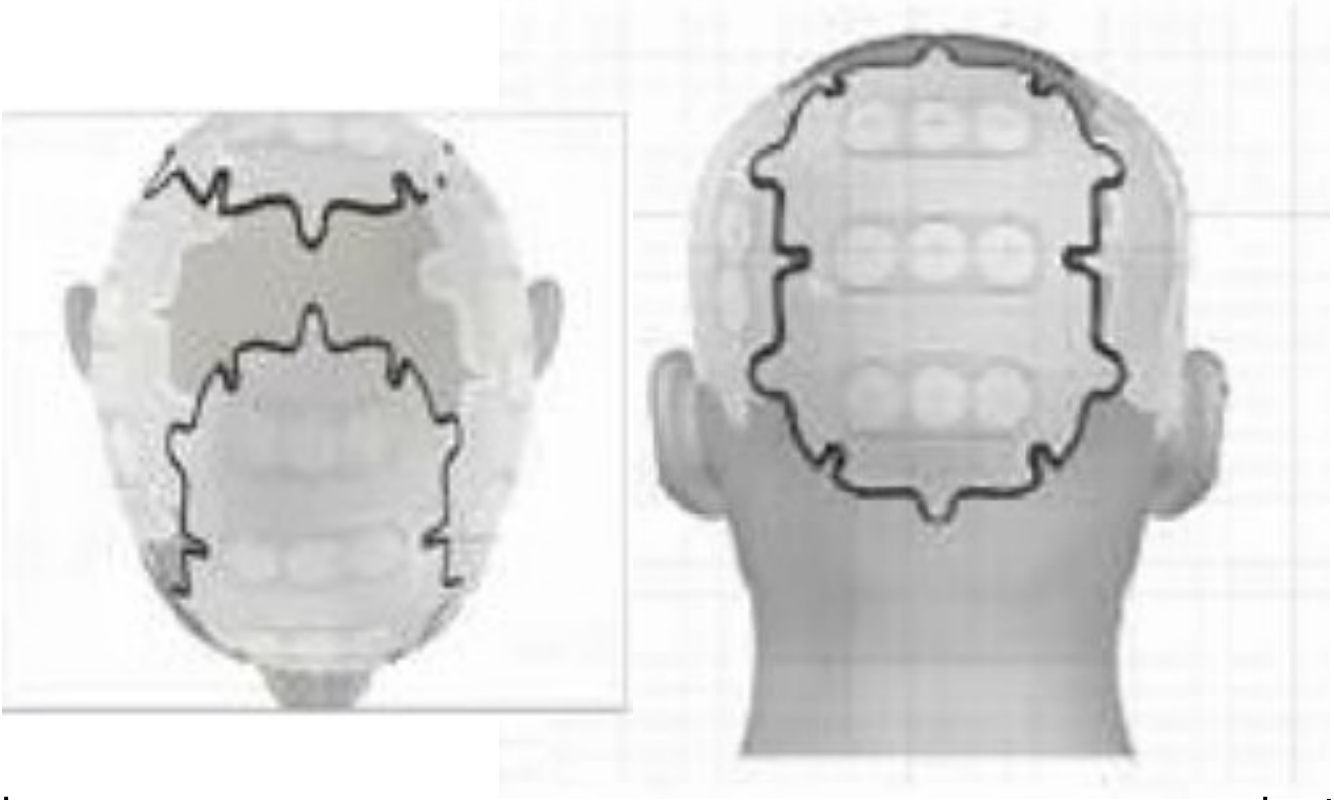
Adjuvant TMZ

+ 200 kHz
TTFields

?

Dr Patel: Case 3

- 27 y.o. man with brainstem lesion ×3 years presenting for second opinion after interval worsening of cranial neuropathies (cranial nerves 7 and 8).
- s/p concurrent chemoradiation with temozolomide (TMZ)
- Plan for adjuvant TMZ + 200 kHz TTFields with modified layout (off-label) based on 2017 computational modeling



Standard layout for **supra**tentorial glioblastoma

Off-label layout for **infra**tentorial glioblastoma

Bomzon, Novocure Data on File OPT-132, 2017

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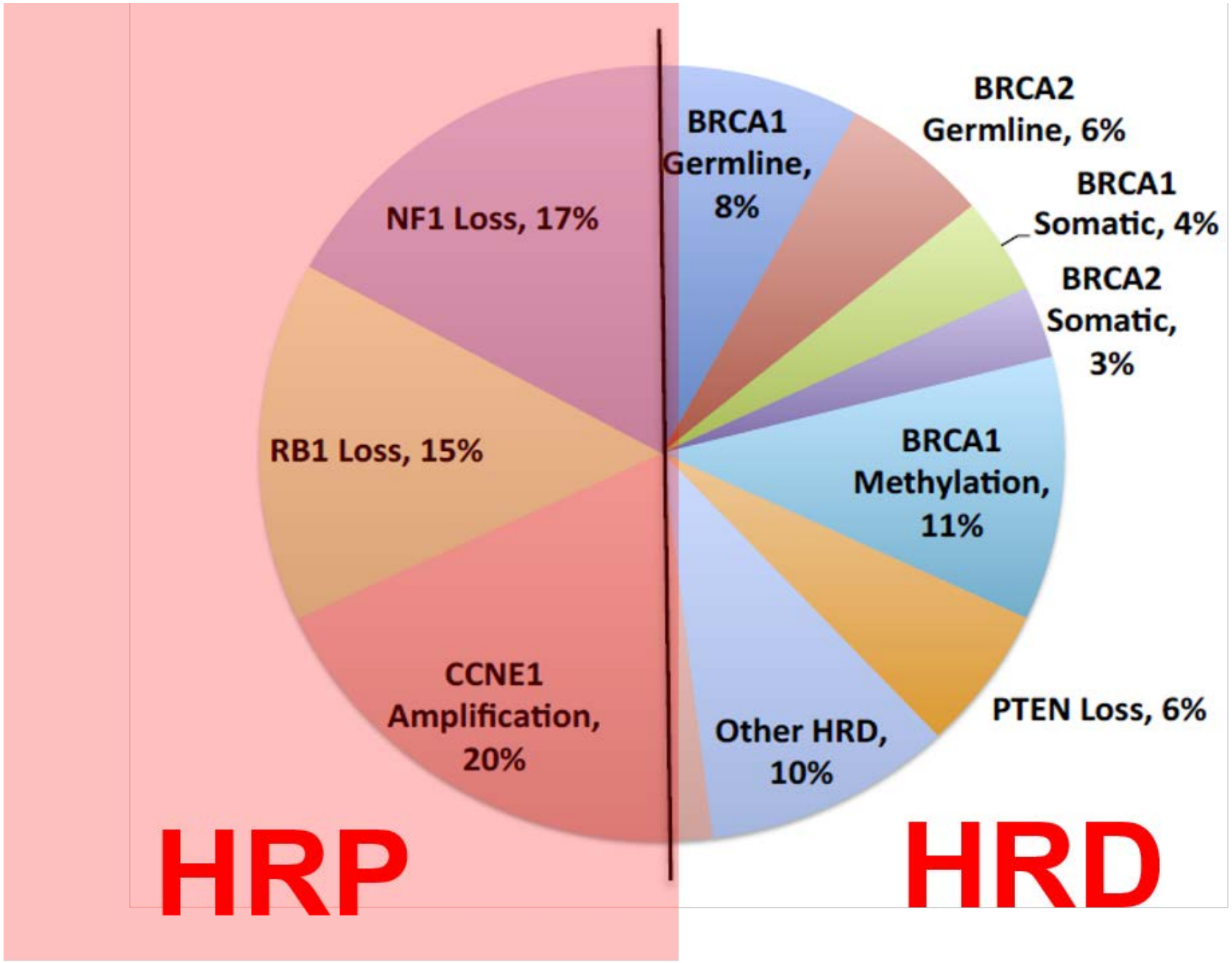
RTP RESEARCH TO PRACTICE

Dr. Konecny – CASE 1

History of Presenting Illness:
60 y.o. female with stage IIIC high grade serous carcinoma.

3/2021: Endometrial biopsy done for AUB, negative for malignancy, proliferative endometrium seen
4/2021: For markedly enlarged fibroid uterus, recommended ex-lap
5/2021: Ex-lap, TAH, BSO, omentectomy and optimal tumor debulking surgery.
6/2021 – 10/2021: 6 x carboplatin/paclitaxel + bevacizumab
7/2021: Tested positive for germline BRCA2 mutation (c.5722_5723del, premature truncation of the BRCA2 protein at amino acid position 1909)
11/2021: Started olaparib 300 mg BID - due to severe fatigue, low appetite, weight loss, mucositis, dry eyes, constipation and anemia requiring two blood transfusions dose was reduced to 150 mg BID.
10/2022: Completed bevacizumab and continuing with olaparib 150 mg BID


BRCA1 Germline, 8%
BRCA2 Germline, 6%
BRCA1 Somatic, 4%
BRCA2 Somatic, 3%
BRCA1 Methylation, 11%
PTEN Loss, 6%
Other HRD, 10%
CCNE1 Amplification, 20%
RB1 Loss, 15%
NF1 Loss, 17%
HRP
HRD

PARP Inhibitors in Ovarian Cancer

Population	Phase	Upfront maintenance	Plat Sens Rec (maintenance post chemo)	Plat Sens Rec (treatment)	Plat Res Rec (treatment)
BRCA mutated	III	SOLO-1 (olaparib)	SOLO-2 (olaparib)	SOLO-3 (olaparib vs chemo) XXX ARIEL4 (rucaparib v chemo) XXX	
	II			ARIEL2 (rucaparib#)	
(*BRCAm or HRD)	III	PAOLA-1 (olaparib/bev*)		QUADRA (niraparib*¤)	QUADRA (niraparib*) XXX
All Comers	III	VELIA (veliparib) PRIMA (niraparib) ATHENA-MONO (rucaparib)	Study 19 (olaparib) NOVA (niraparib@) ARIEL3 (rucaparib)	AVANOVA2 (niraparib+/-bev) GY-004 (olaparib +/- cediranib)	
	II	OVARIO (niraparib/bev)			

ΔΔΔ ???

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¤QUADRA single arm w/o comparator, niraparib withdrawal by GSK: (9/6/22)

??? 11/2022 FDA request to restrict rucaparib to BRCAmut patients only

ΔΔΔ 11/2022 FDA approval restricted to gBRCAmut patients only

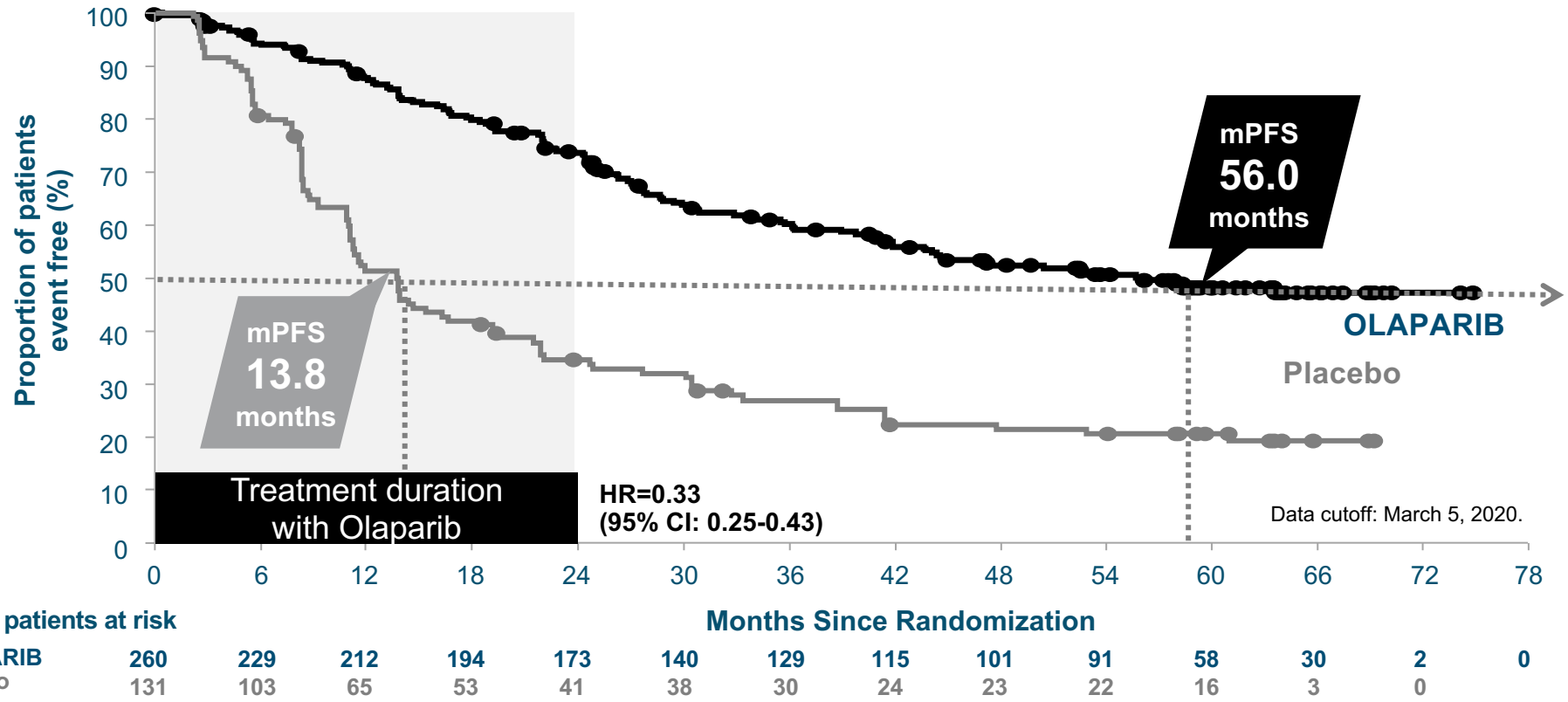
SOLO-1: Primary Analysis and Post Hoc 5-Year Follow-up Analysis

Primary analysis: median PFS

Olaparib
(N=260)
Not reached

Placebo
(N=131)
13.8 months

HR=0.30
(95% CI: 0.23-0.41); *P*<0.0001



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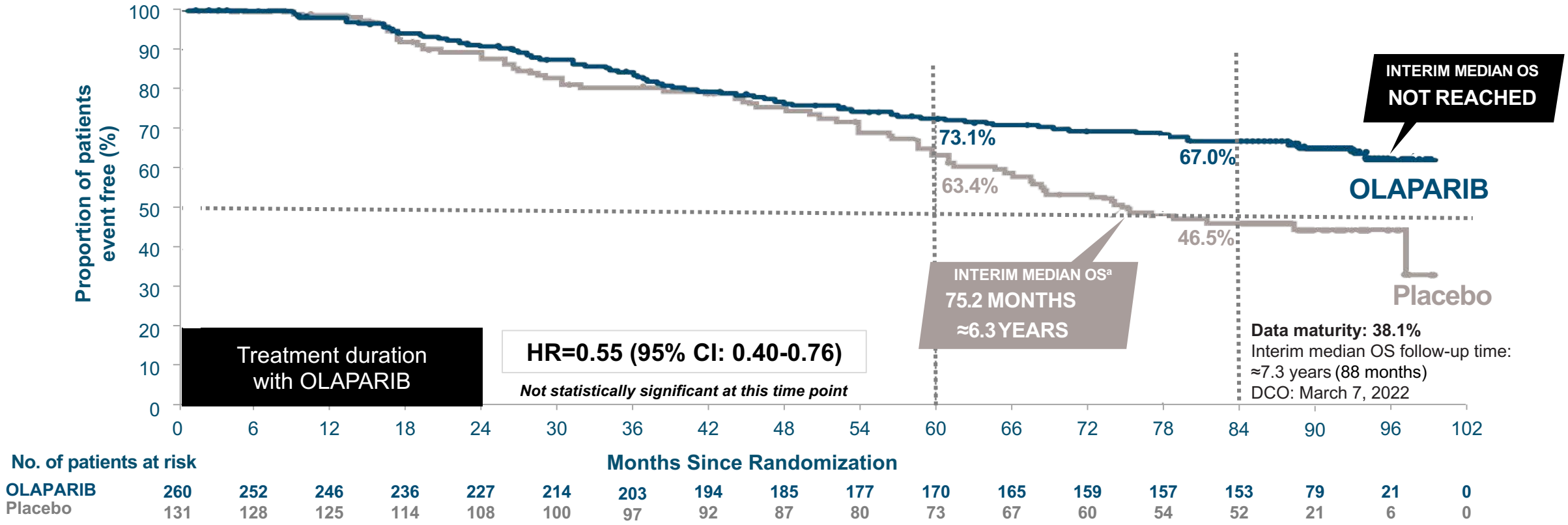
Moore K, et al. *N Engl J Med.* 2018;379(26):2495-2505. 3. Banerjee S, et al. *Lancet Oncol.* 2021;22(12):1721-1731.

SOLO-1 Prespecified Descriptive 7-Year Interim OS Analysis

44.3% of patients in the placebo arm and 14.6% in the Olaparib arm received subsequent PARPi therapy



No. of patients at risk

OLAPARIB	260	252	246	236	227	214	203	194	185	177	170	165	159	157	153	79	21	0
Placebo	131	128	125	114	108	100	97	92	87	80	73	67	60	54	52	21	6	0

UCLA Health

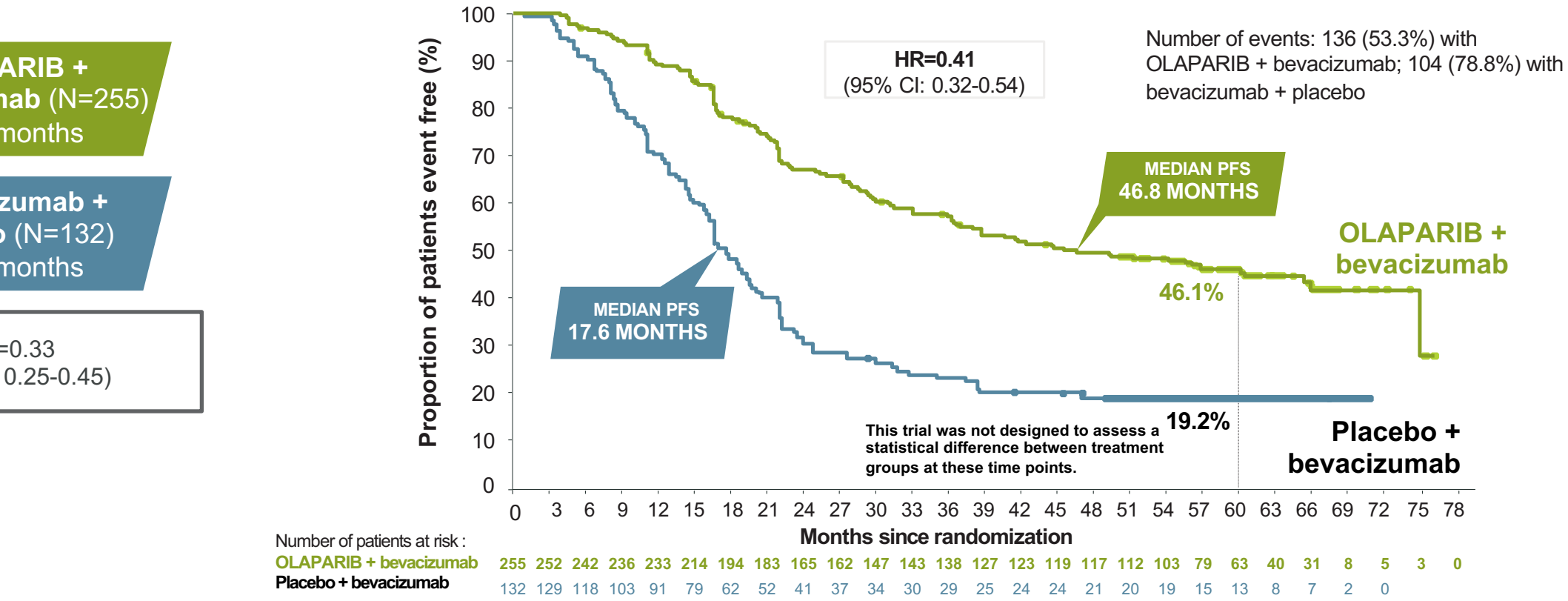
DiSilvestro P, et al. *J Clin Oncol*. DOI: https://doi.org/10.1200/JCO.22.01549.

PAOLA-1 Primary Analysis and Prespecified 5-Year Follow-up Analysis

OLAPARIB + bevacizumab (N=255)
37.2 months

Bevacizumab + placebo (N=132)
17.7 months

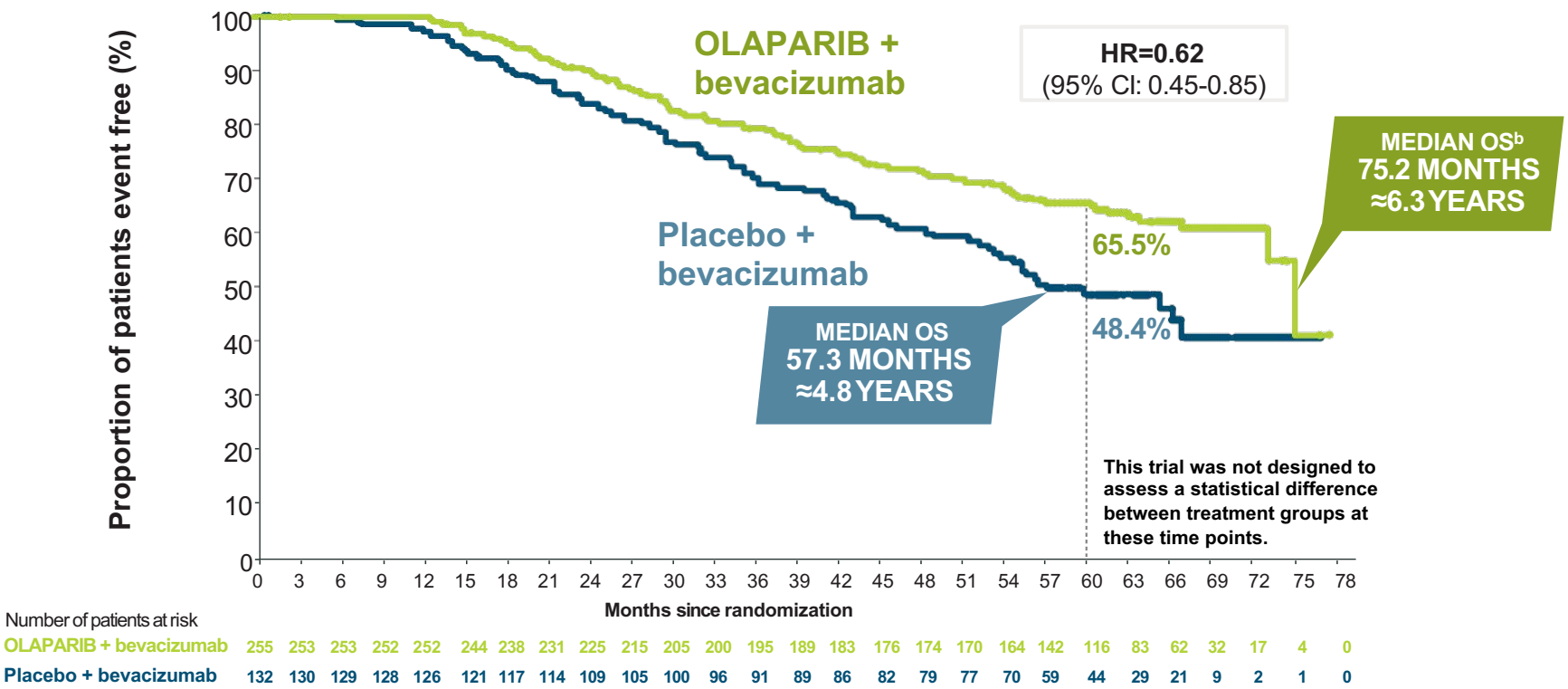
HR=0.33
(95% CI: 0.25-0.45)



UCLA Health

Ray-Coquard I, et al. *N Engl J Med*. 2019;381(25):2416-2428. 2. Ray-Coquard I, et al. Presentation at: ESMO Congress; September 9-13, 2022; Paris, France.Presentation LBA29. 3. Ray-Coquard I, et al. Supplementary appendix. *N Engl J Med.* 2019;381(25):2416-2428.

PAOLA-1—Prespecified 5-Year Follow-up OS Analysis in HRD-Positive Patients



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MDS/AML in Randomized Ovarian Cancer PARP Inhibitor Maintenance Trials

			PARPi	MDS/AML Events by arm	
Trial	Setting	Agent	Duration	PARPi, n (%)	Comparator, n (%)
SOLO-1[4]	1L maint	Olaparib	2 years	3/260 (1.5)	1/130 (0.8)
PRIMA[6]	1L maint	Niraparib	3 years	1/484 (<1)	0/244
PAOLA-1[5]	1L maint	Olaparib	2 years	6/535 (1)	1/267 (0.4)
ATHENA MONO[9]	1L maint	Rucaparib	2 years	2/425 (0.5)	0/110
Study19[8]	PS maint	Olaparib	UDP, 18% >3yrs	2/136 (1.5)	1/129 (<1)
SOLO-2[2]	PS maint	Olaparib	UDP, mean 29.1 mos	16/195 (8)	4/99 (4)
NOVA[3]	PS maint	Niraparib	UDP	13/367 (3.5)	3/179 (1.7)
gBRCAm				9/136 (6.6)	2/65 (3.1)
non-gBRCAm				4/231 (1.7)	1/114 (0.9)
ARIEL3[7]	PS maint	Rucaparib	UDP, median 8.3 mos	14/375 (3.8)	6/189 (3.2)
PARPi ≥24m[10]				9/79 (11.4)	
non-gBRCAm				5/245 (2.0)	1/123 (0.8)
gBRCAm				9/130 (6.9)	3/63 (4.8)
PARPi ≥24 mos				7/46 (15.2)	

[2]Poveda A, et al. Lancet Oncol 2021, [3]Matulonis U. et al. SGO 2021, [4]DiSilvestro P, et al. J Clin Oncol 2022, [5]Ray-Coquard I et al. NEJM Dec 2019, [6]Gonzalez-Martin A et al. NEJM 2019, [7]Coleman RL et al. IGCS 2022, [8]Lederman J et al. Lancet 2016 17: 1579-89, [9]Monk B et al. J Clin Oncol 2022, [10]O'Malley et al. Gyn Onc 10/2022

Agenda

Tumor Treating Fields

MODULE 1: Tumor Treating Fields with Dr Chirag Patel

- Mechanism of action of tumor treating fields
- Tumor treating fields in glioblastoma multiforme
- Tumor treating fields in other tumor types
- Case presentations

PARP Inhibitor Therapy in Ovarian Cancer

MODULE 2: Updates on PARP Inhibitors in 2023 with Dr Gottfried Konecny

- PARP inhibitors as up-front maintenance therapy for ovarian cancer
- PARP inhibitors for recurrent ovarian cancer

PARP Inhibitors in Ovarian Cancer

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Year in Review: Clinical Investigator Perspectives on the Most Relevant New Data Sets and Advances in Oncology

A Multitumor CME/MOC-Accredited Live Webinar Series

Prostate Cancer

Wednesday, March 1, 2023
5:00 PM – 6:00 PM ET

Faculty

Tanya B Dorff, MD

A Oliver Sartor, MD

Moderator

Neil Love, MD

RTP Year in Review 2023

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CME and MOC credit information will be emailed to each participant within 5 business days.

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