

CREATING BREAKTHROUGH DRUGS
TO TREAT BRAIN DISEASES AND FIGHT CANCER

~ ANG1005 ~
Targeting LRP-1 in Brain Cancer

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angiochem



Treatment options are limited, in part due to the difficulties associated with drug delivery across the BLOOD-BRAIN BARRIER (BBB)

- **Brain Metastases:** Up to 180,000 cases per year in the US, mostly from lung and breast cancers
 - Standard of care includes surgery and radiotherapy
 - No standard of care at the time of recurrence
 - Median survival is very poor
- **Malignant Gliomas:** 18,000 new cases per year in the US alone
 - Despite standard treatment, median survival is only 12-15 months for patients with GBM, and 2-5 years for patients with anaplastic gliomas

- **Solid tumor with Progressive Brain Metastases: 56 patients**
- **Recurrent Glioma: 63 patients**

PRIMARY OBJECTIVES

- Characterize safety and tolerability
- Identify maximum tolerated dose (MTD)

SECONDARY OBJECTIVES

- Pharmacokinetics
- Immunogenicity of ANG1005
- To determine preliminary efficacy



119 Patients Treated from US Sites

Brain Metastases Study Sites

MD Anderson Cancer Center, Houston, TX

~ Dr. Razelle Kurzrock

Cancer Therapy Research Center, San Antonio, TX

~ Dr. John Sarantopoulos

Gabrail Cancer Center, Canton, OH

~ Dr. Nashat Gabrail

Recurrent Glioma Study Sites

Dana Farber Cancer Institute,

Beth Israel Deaconess Medical Center,

Massachusetts General Hospital, Boston, MA

~ Dr. Jan Drappatz

Cancer Therapy Research Center, San Antonio, TX

~ Dr. Andrew Brenner

Columbia University Medical Center, New York, NY

~ Dr. Steven Rosenfeld

MD Anderson Cancer Center, Houston, TX

~ Dr. Morris Groves

Henry Ford Health System, Detroit, MI

~ Dr. Tom Mikkelsen

University of Virginia Health System,
Charlottesville, VA

~ Dr. David Schiff

- **Dose levels from 30 to 700 mg/m²**
 - MTD is 650 mg/m², IV infusion once every 21 days
- **No toxicity related to the EPiC platform**
 - No evidence of CNS toxicity
 - No antibody production (dosing up to 18 cycles)
- **Favourable tolerability profile**
 - AEs of highest frequencies are of hematological origin:
 - neutropenia (58% $<1.5 \times 10^9$ /L), leucopenia (59% $<3.0 \times 10^9$ /L), anemia (33% Hg <10.0 g/dL)
 - The most common non-hematological AEs (all severities) are:
 - fatigue (31%), peripheral neuropathy (23%), alopecia (22%), nausea (20%), mucositis (14%), diarrhea (13%), rash (13%), infusion reactions (12%).

Brain Metastases Study

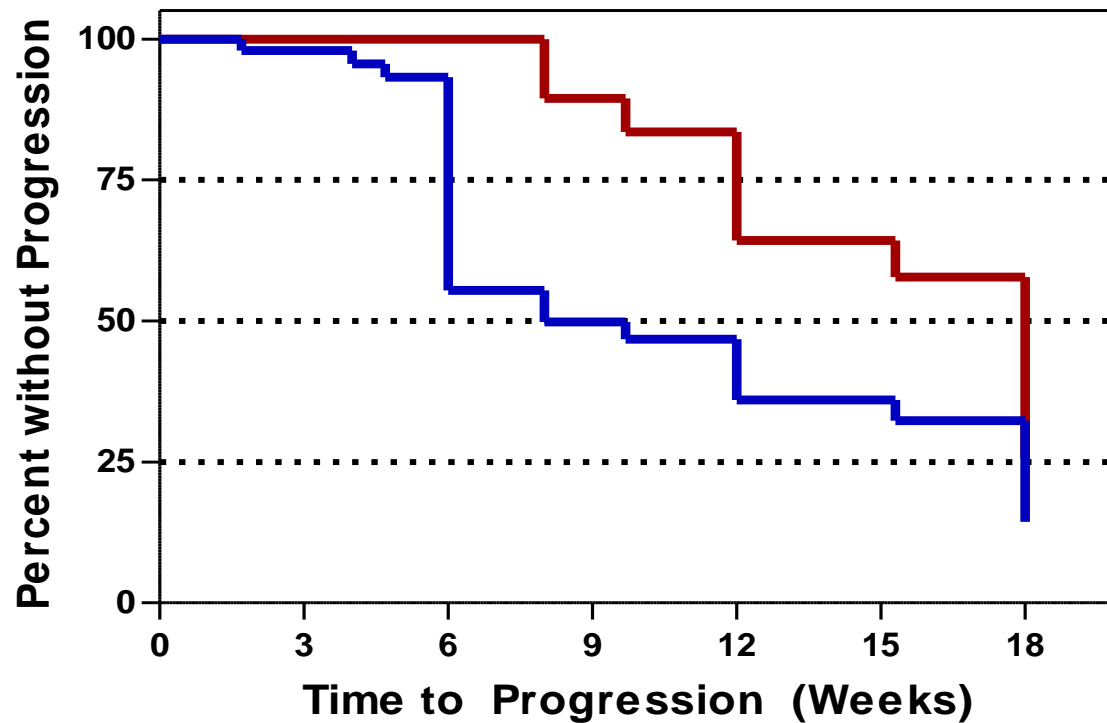
~ Summary of Overall Best Response

Dose (mg/m ²)	420-700 mg/m ²	Prior Taxane Failures*
Sample Size (n=33)	n=21	n=12
CR		
PR	5	4
MR	6	5
SD	4	1
PD	6	2
% ≥ SD	71%	83%

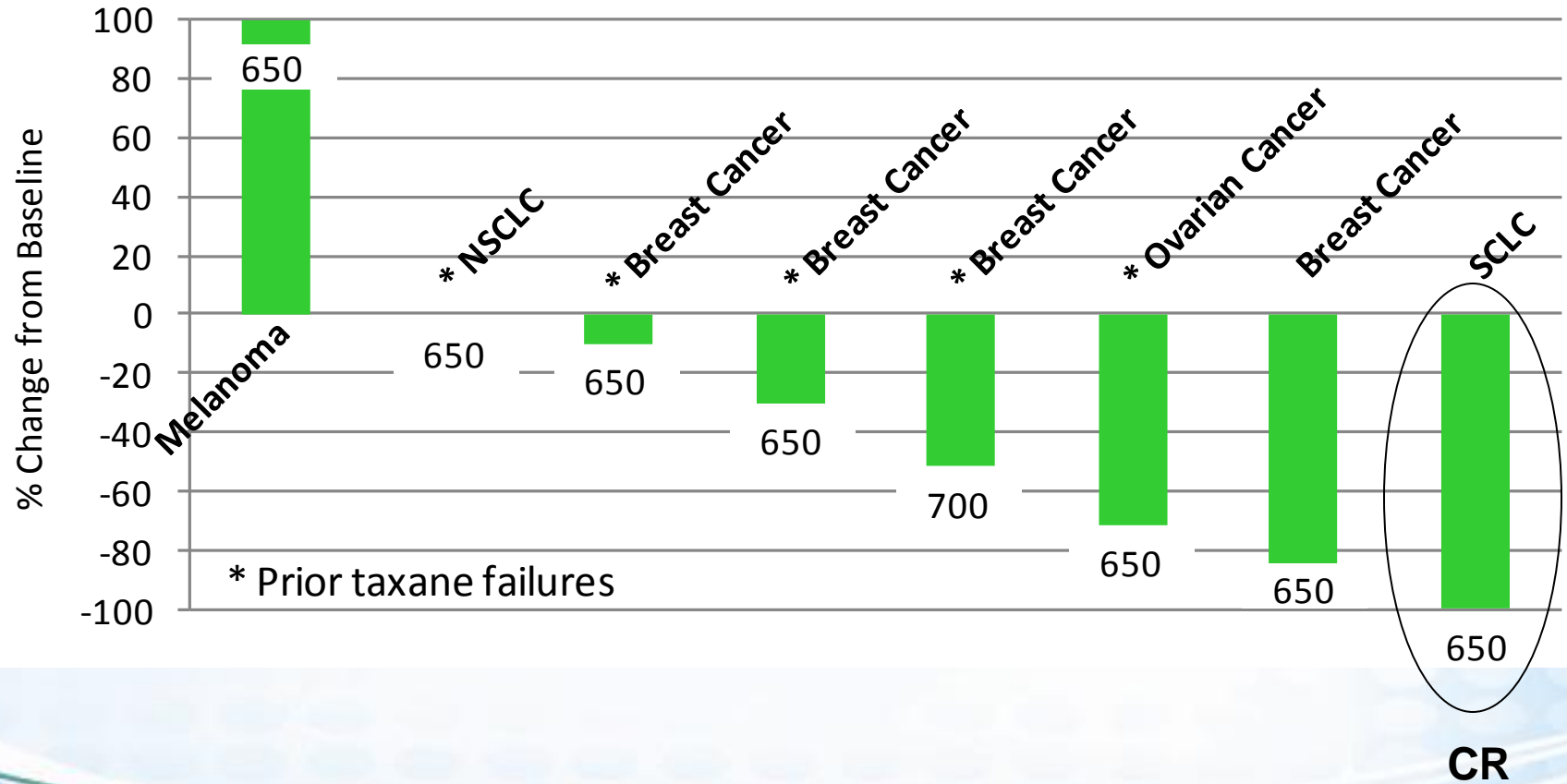
*Patients treated at 420-700mg/m² group

CR=Complete Response; PR=Partial Response; MR=Minor Response; SD=Stable Disease; PD=Progressive Disease

KAPLAN-MEIER CURVES OF MEDIAN TTP
ALL PATIENTS VS. RESPONDERS (\geq SD)
 Doses 30-700 mg/m²

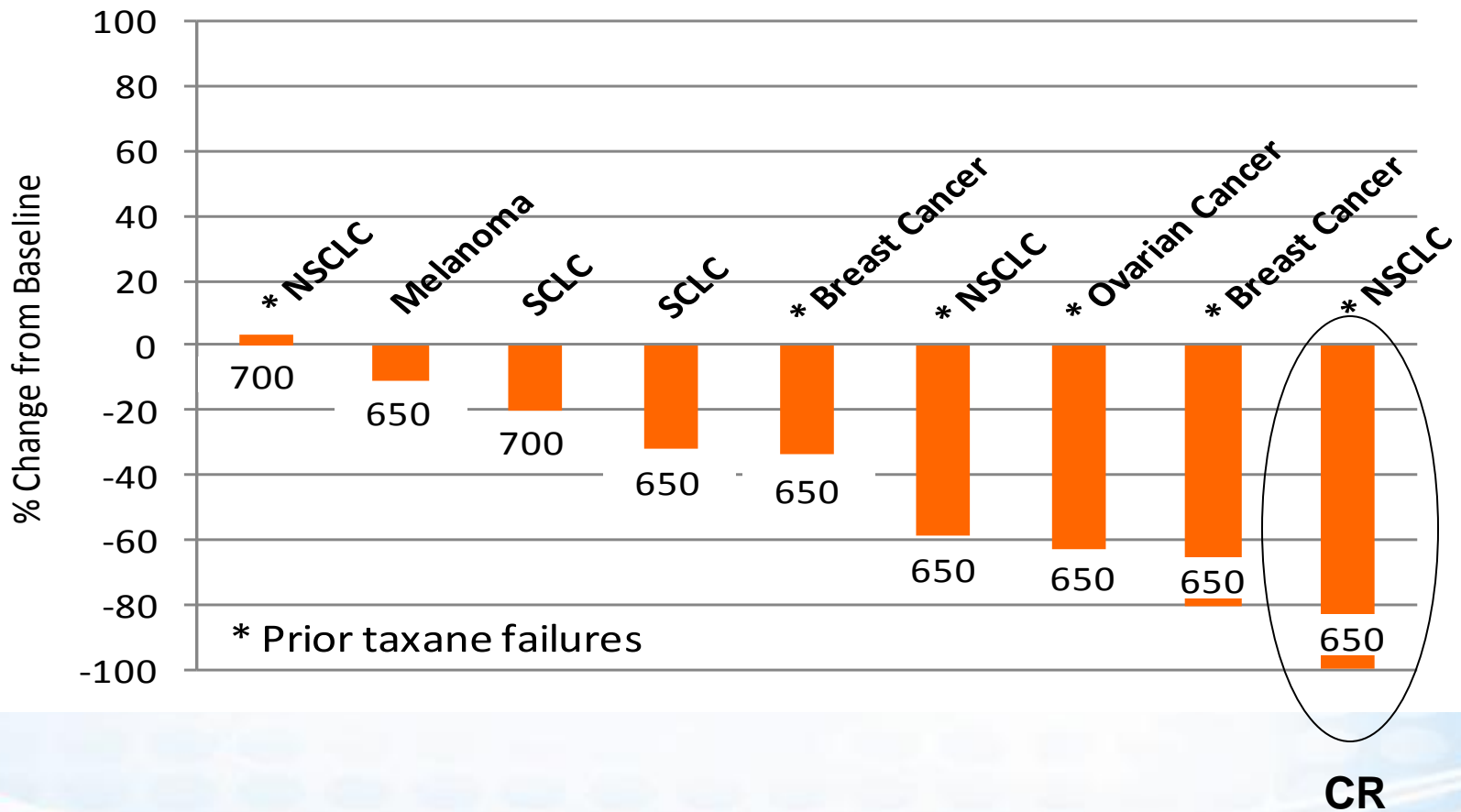


Response - Liver Metastases Responders# Dosed ≥ 420 mg/m²



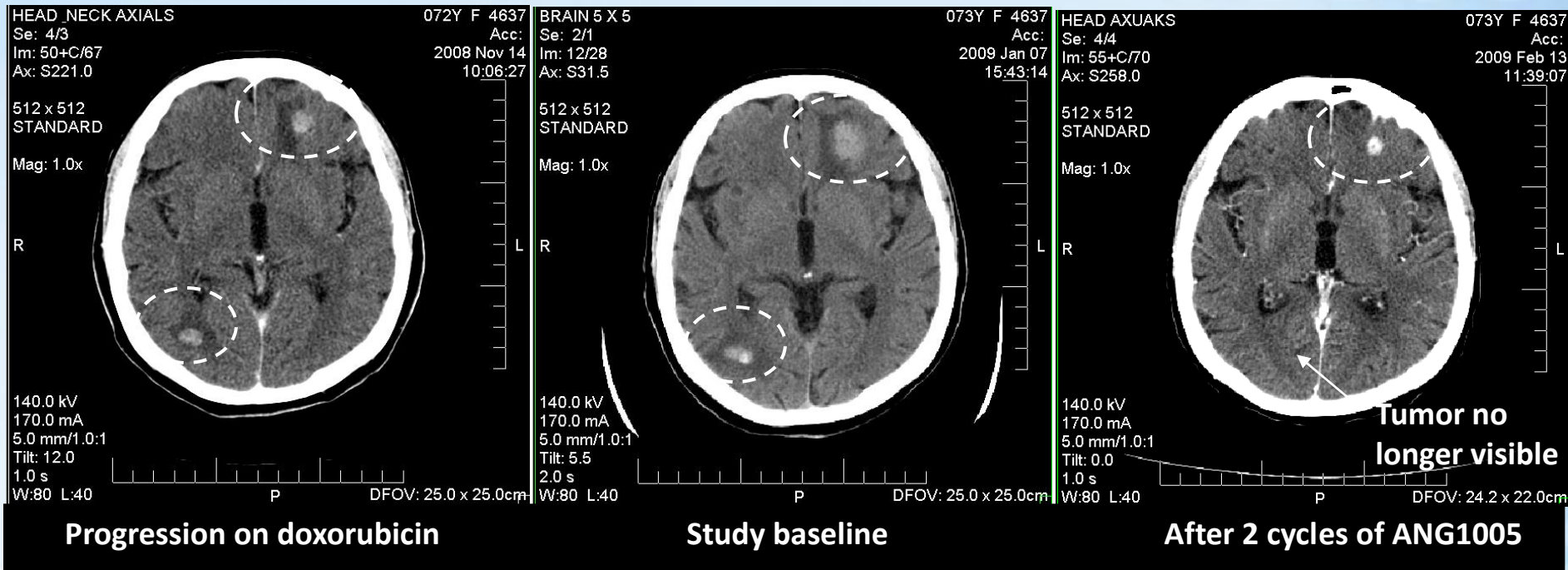
Patients that had an OVERALL best response of stable disease or better

Response - Lung Metastases Responders# Dosed ≥ 420 mg/m²



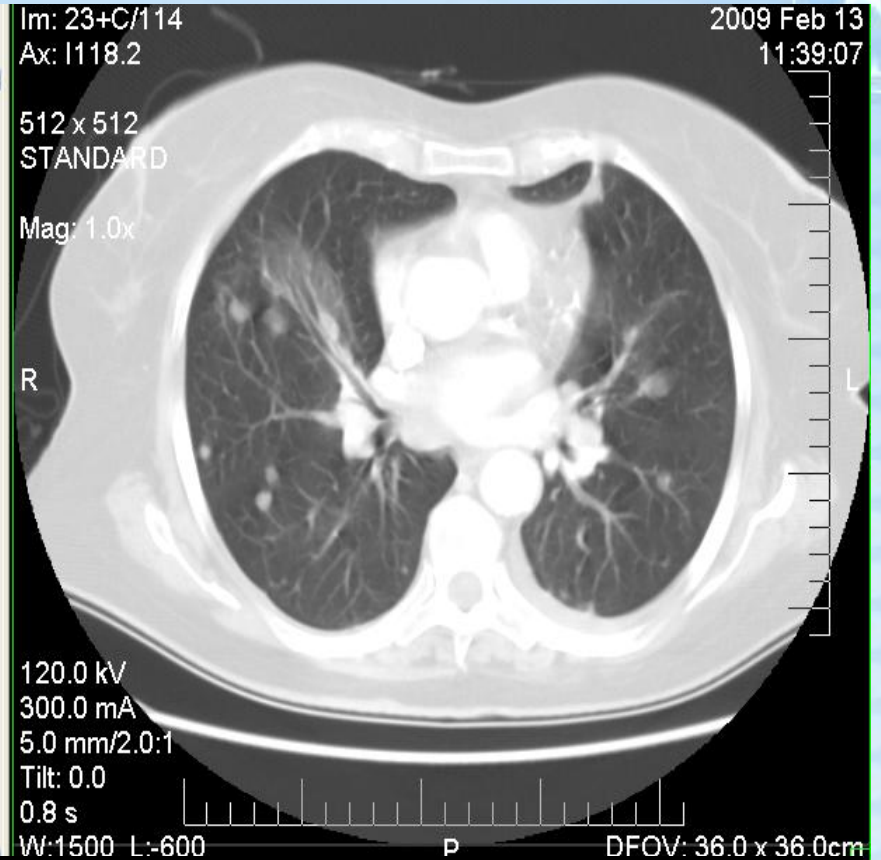
Patients that had an *OVERALL* best response of stable disease or better

73 y.o. female with metastases originating from taxane-resistant ovarian cancer





Study baseline



After 2 cycles of ANG1005

Recurrent Glioma Study ~ Summary of Best Response

Dose	300-700 mg/m ²
Sample Size (n=46)	n=28
CR	2
PR	2
MR	11
SD	2
PD	11
% ≥ SD	61%

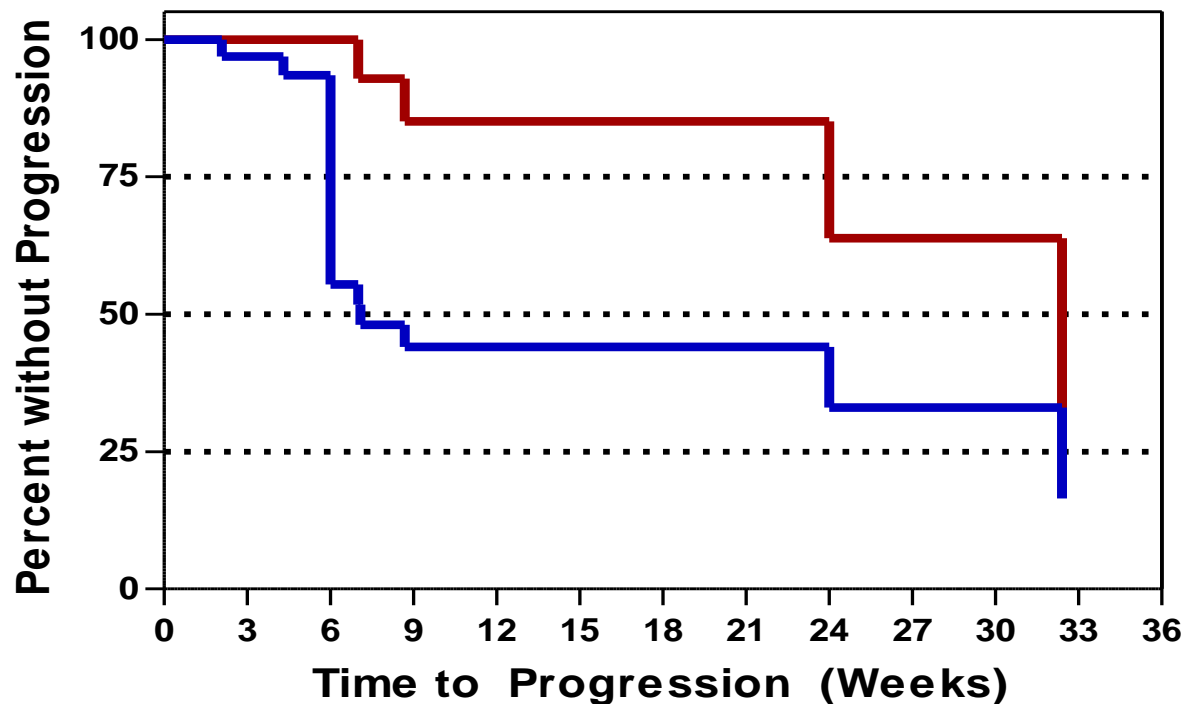
CR=Complete Response; PR=Partial Response; MR=Minor Response; SD=Stable Disease; PD=Progressive Disease

Recurrent Glioma Study ~Durability of Responses

KAPLAN-MEIER CURVES OF MEDIAN TTP

ALL PATIENTS VS. **RESPONDERS (\geq SD)**

Doses 300-700 mg/m²



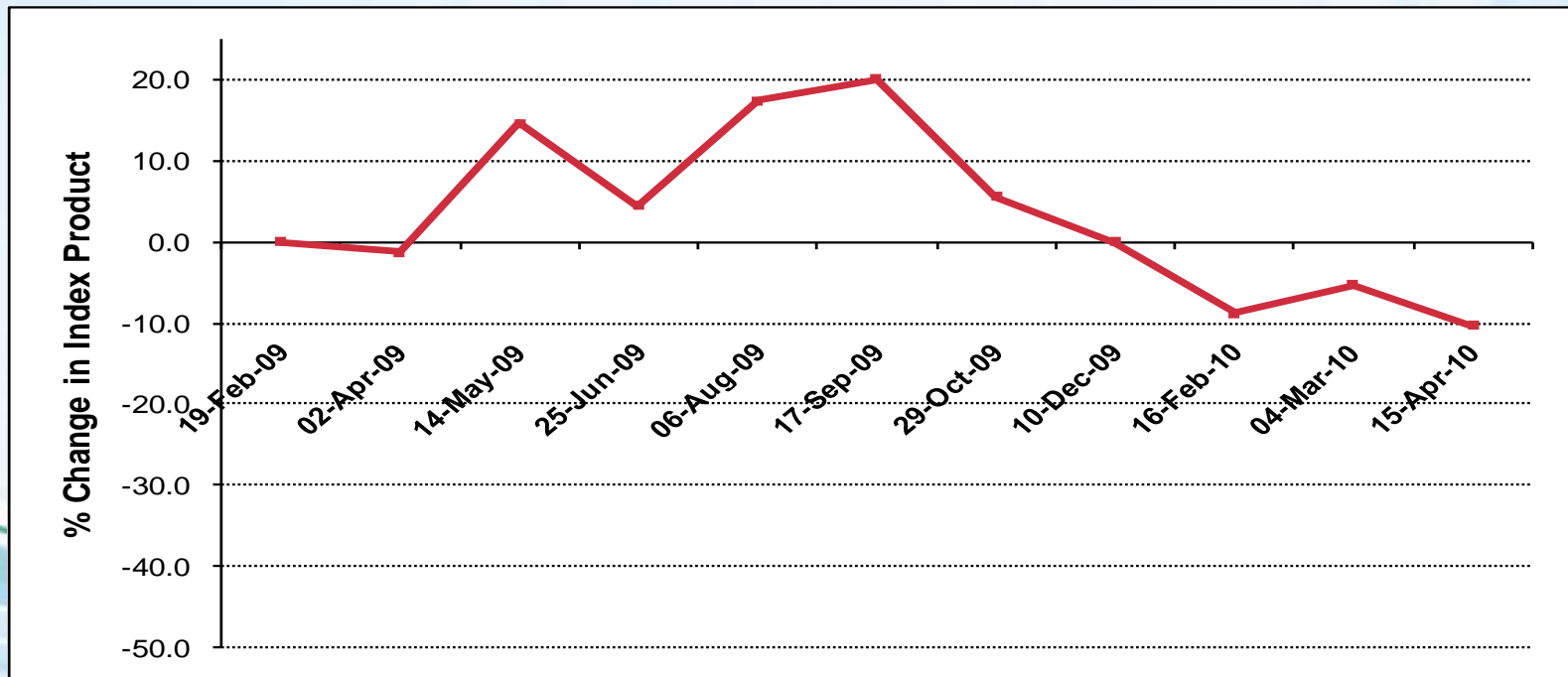
Tumor Extraction Results



Sample	#1	#2	#3	#4	#5	#6	#7
Dose Level (mg/m ²)	200	300	420	550	550	550	550
Extraction Time (h)	~4.0	~5.0	~4.0	~4.5	~6.0	~4.5	~5.5
Plasma ANG1005 (μM)	34.3	34.4	53.5	100.1	56.5	63.0	81.0
Tumor ANG1005 (μM)	2.8	9.4	7.0	23.0	98.0	238.2	31.5
[Tumor]:[Plasma]	8.2%	27.3%	13.3%	23.0%	173%	379%	38.9%

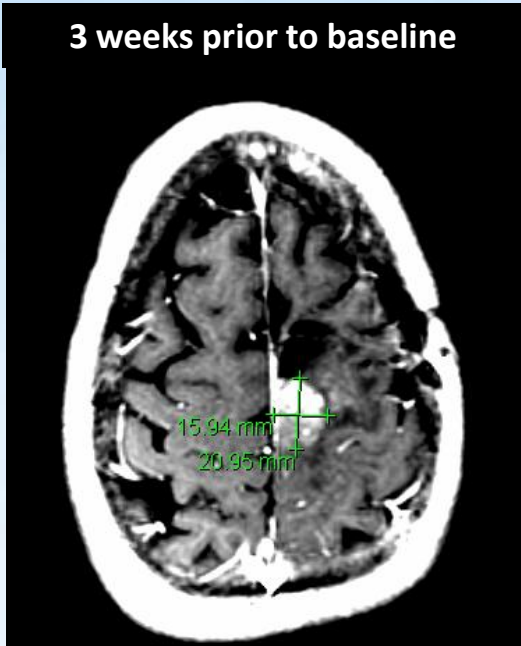
Bevacizumab Refractory Patient:

- 51 y.o M with GBM
- Treated with TMZ/RT upfront followed by Bev/CPT-11 for 1st recurrence
- Received 22 cycles of ANG1005 for 2nd relapse
- Patient remains progression free, PFS = 15+ months
- Tumor measurements over time:



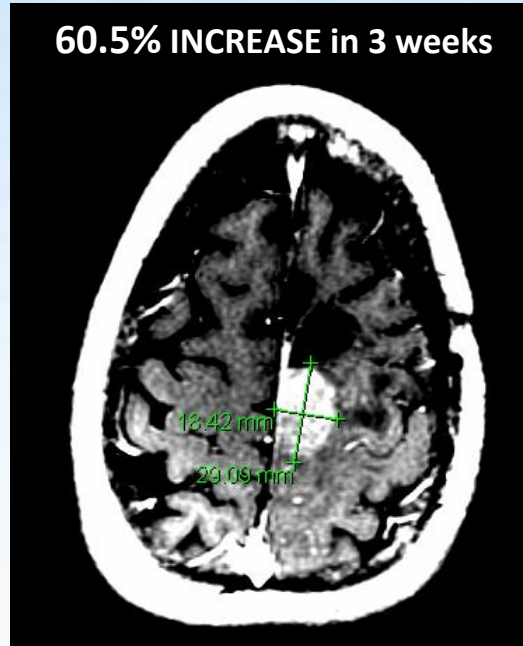
49 y.o. female patient with anaplastic oligoastrocytoma

3 weeks prior to baseline



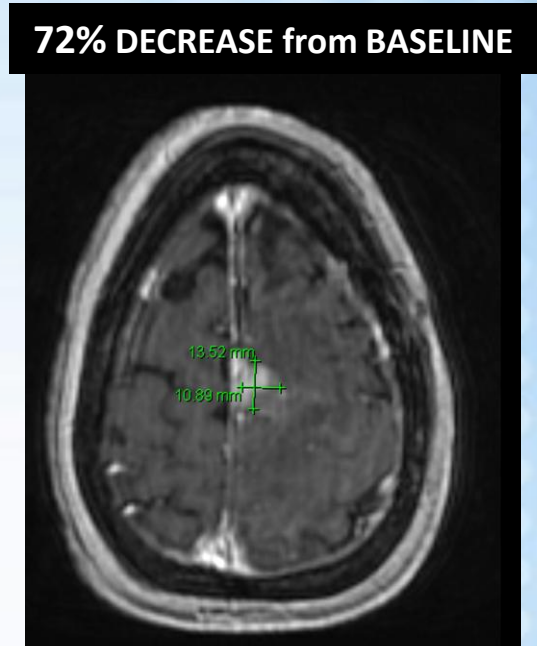
Progression after 1 yr of temozolomide. Prior treatments include radiation, surgery.

60.5% INCREASE in 3 weeks



Study baseline
Rapidly progressive symptoms including left hemiparesis and was using a cane and wheelchair

72% DECREASE from BASELINE



After 8 cycles of ANG1005
Walking unaided

- Well tolerated with no CNS toxicity and no antibody induction
- Encouraging responses in primary and secondary brain tumors
- Reversal of neurological deficits observed in several cases
- Significant tumor reductions also in liver, lung and other organs
- Encouraging response rate in taxane-failure cancers
- Therapeutic concentrations of ANG1005 in brain tumors =
Proof-of-concept validation of the platform technology
- Results warrant further development