

ANTI-INFLAMMATORY EFFECTS OF THE
PIGF NEUTRALIZING ANTIBODY THR-317 IN
PATIENTS WITH DIABETIC MACULAR
EDEMA

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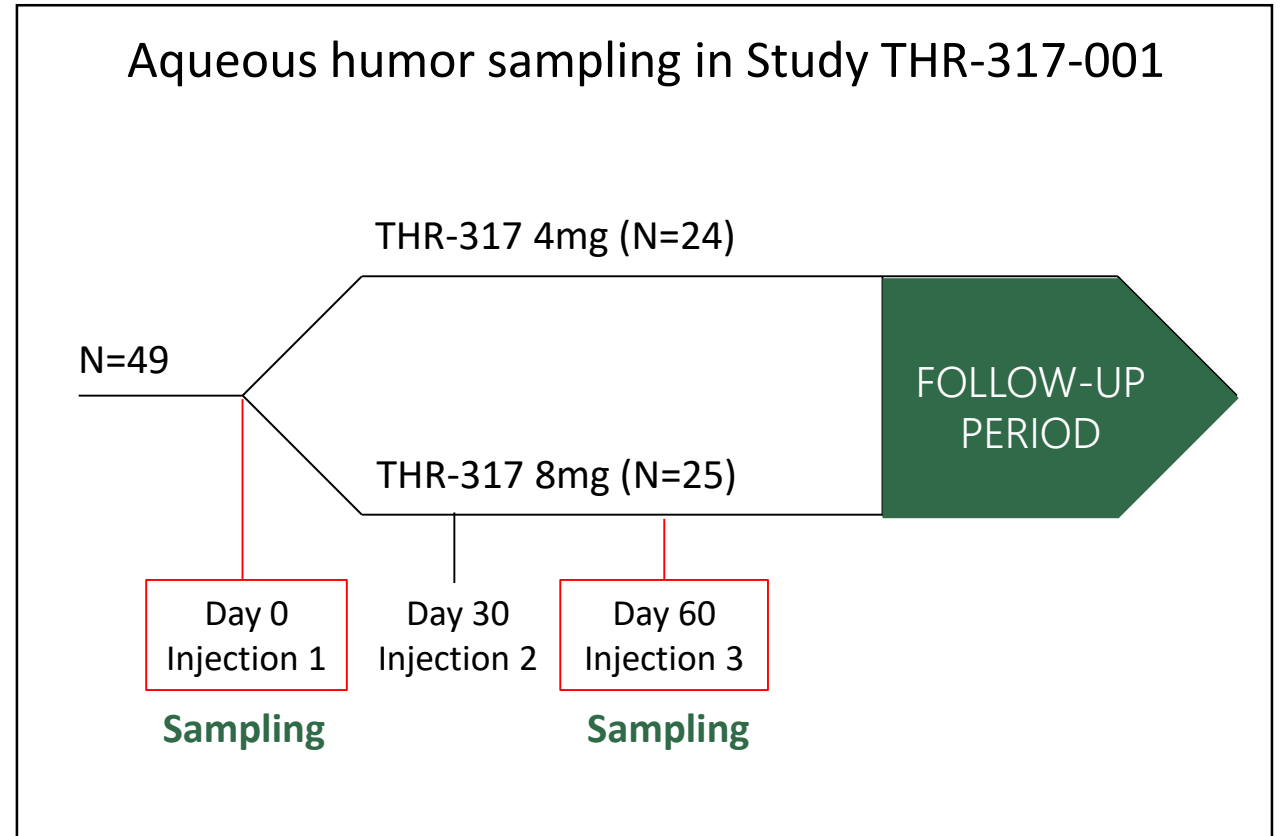


Introduction

- THR-317 (Oxurion NV) is a monoclonal antibody targeting placental growth factor (PlGF)
- Preclinical animal models demonstrated ⁽¹⁾ that anti-PlGF
 - ⇒ reduces retinal neovascularization and vascular leakage
 - ⇒ reduces retinal inflammation and fibrosis,
 - ⇒ in contrast to anti-VEGF, does not elicit a degenerative response in retinal ganglion cells
- THR-317 is in clinical development for the potential treatment of Diabetic Macular Edema (DME)

Collection of aqueous humor samples in Study THR-317-001

- Safety and efficacy of three monthly intravitreal injections of THR-317 ⁽¹⁾
- Six anti-VEGF treatment-naïve study participants consented to sampling
 - ⇒ 2 patients receiving 4mg dose
 - ⇒ 4 patients receiving 8mg dose
- Aqueous humor was sampled prior to intravitreal injections of THR-317
 - ⇒ Day 0 (prior 1st injection)
 - ⇒ Day 60 (prior 3rd injection)



OLINK inflammation assay

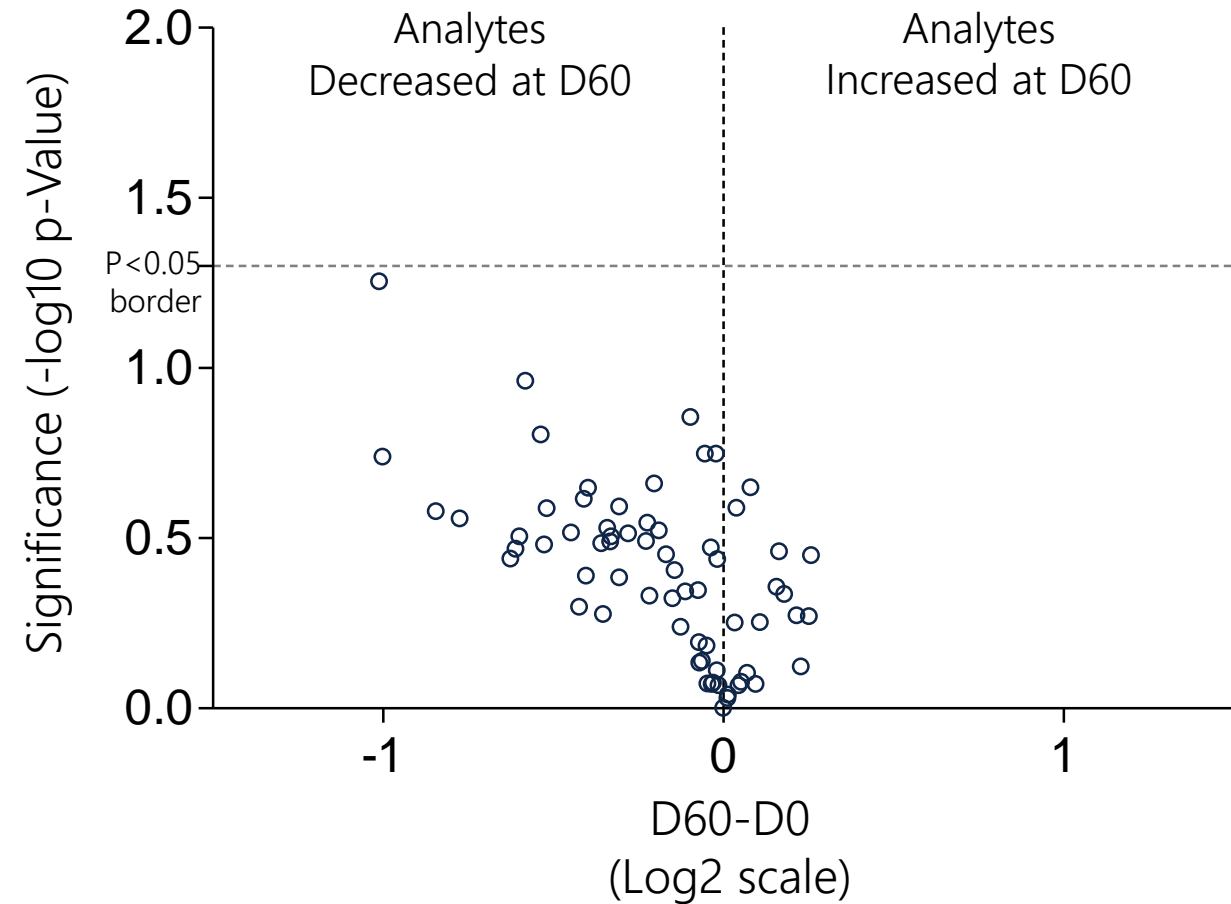
High multiplex measurement of 92 inflammation-related proteins in THR-317-001 aqueous humor samples

IL-8	CXCL1	TRANCE	IL-4
VEGFA	TTSLP	HGF	LIF
BDNF	CCL4	IL-12B	NRTN
MCP-3	CD6	IL-24	MCP-2
GDNF	SCF	IL-13	CASP-8
CDCP1	IL-18	ARTN	CCL25
CD244	SLAMF1	MMP-10	CX3CL1
IL-17	TGF- α	IL-10	TNFRSF9
OPG	MCP-4	TNF	NT-3
TGF β 1	CCL11	CCL23	TWEAK
uPA	TNFSF14	CD5	CCL20
IL-6	FGF-23	CCL3	ST1A1
IL-17C	IL-10RA	Flt3L	STAMPB
MCP-1	FGF-5	CXCL6	IL-5
IL-17A	MMP-1	CXCL10	ADA
CXCL11	LIF-R	4E-BP1	TNF β
AXIN1	FGF-21	IL-20	CDF-1
TRAIL	CCL19	SIRT2	OSM
IL-20A	IL-25RA	CCL28	IL-2
CXCL9	IL-10RB	DNER	β -NGF
CST5	IL-22RA1	EN-RAGE	CXCL5
IL-2RB	IL-18R1	CD40	IFN- γ
IL-1 α	PD-L1	IL-33	FGF-19

Change from baseline of 92 INFLAMMATORY analytes (Average of 6 patients)

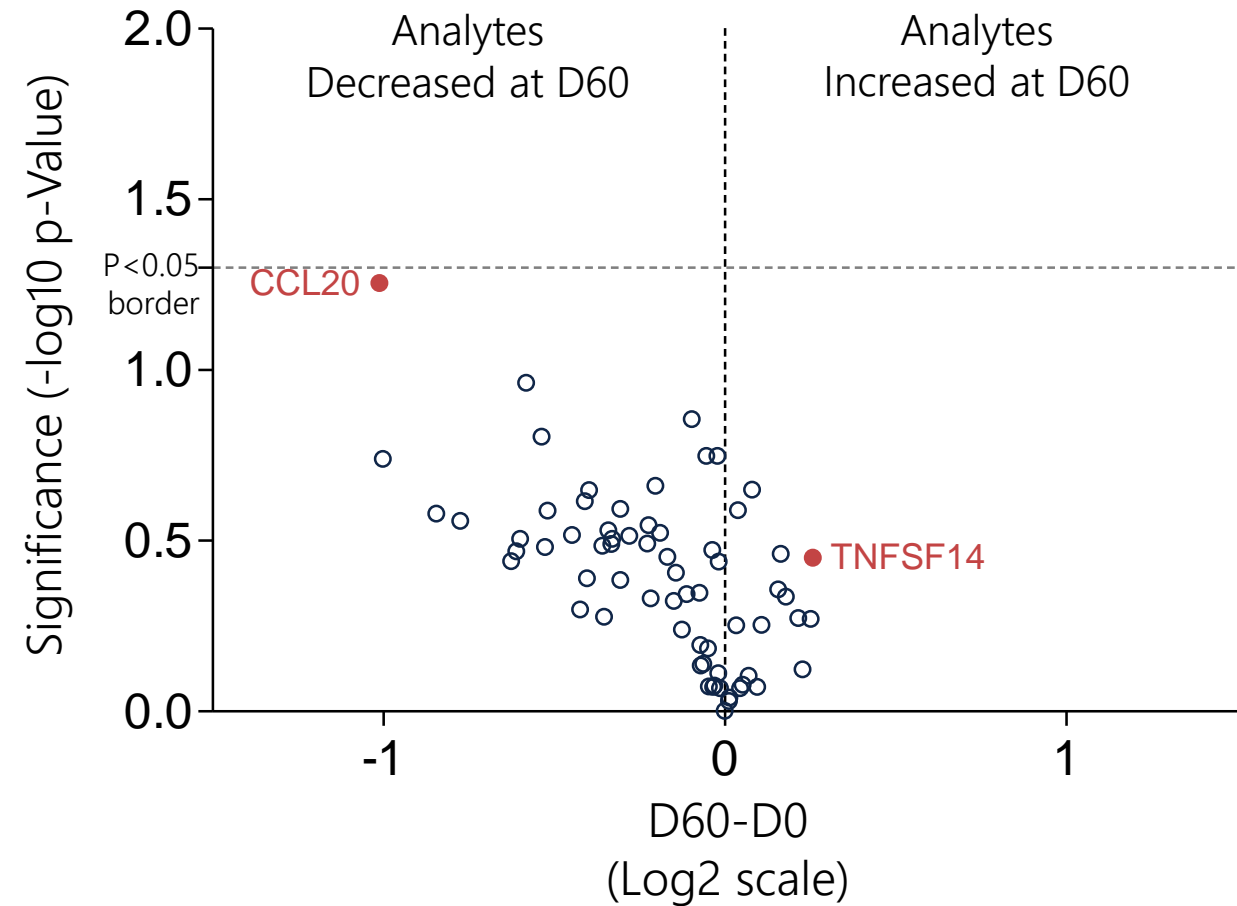
- 718 data points out of 1104 (65%) above LLOQ
- At Day 60 (after 2 injections of THR317):
 - ⇒ 50 analytes decreased
 - ⇒ 17 analytes increased
 - ⇒ 25 analytes not suitable for analysis

- Majority of inflammatory analytes decreased
- However, none reached statistical significance



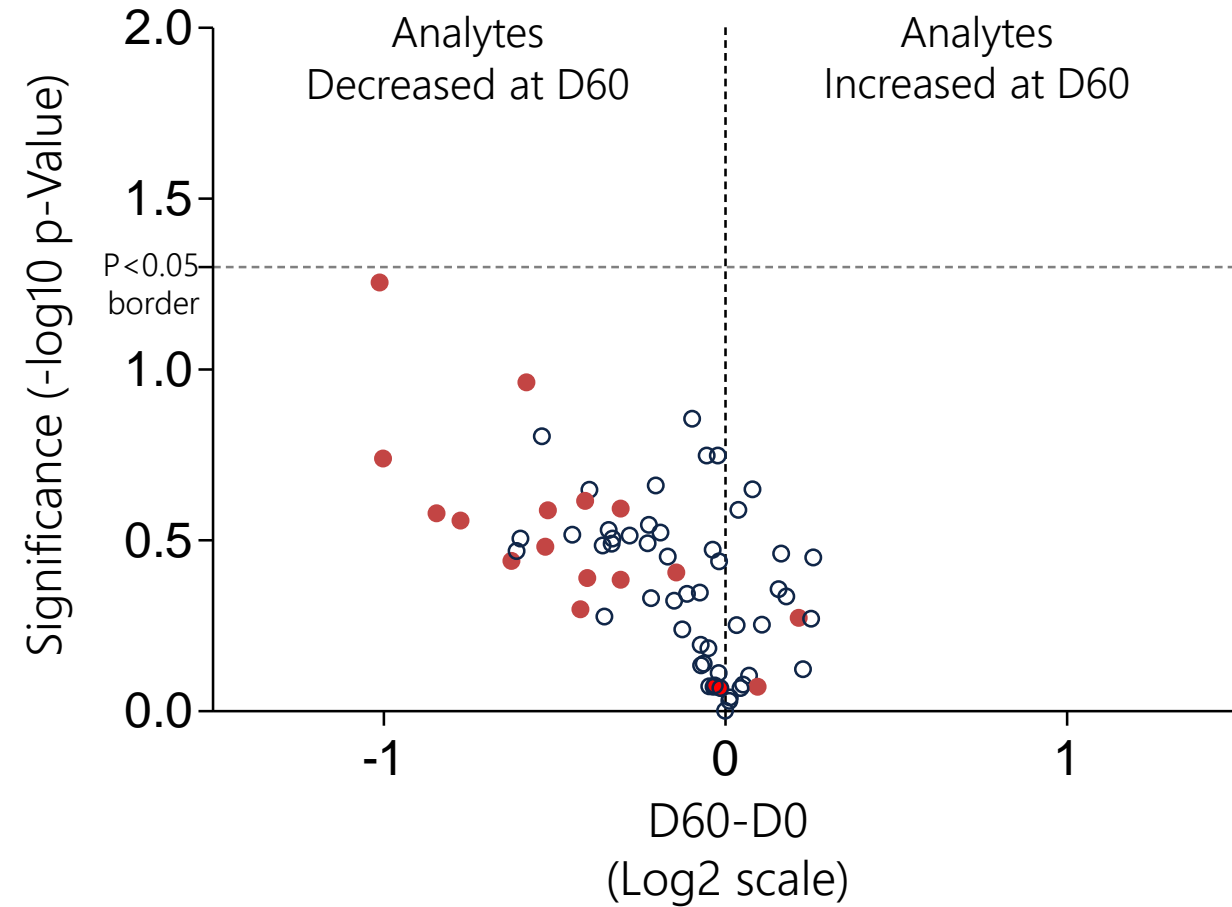
Change from baseline of 92 INFLAMMATORY analytes (Average of 6 patients)

- Strongest decreased analyte = CCL20
 - ⇒ 2.02-fold decrease, uncorrected p-value=0.056
 - ⇒ Attraction of dendritic cells, neutrophils, T-cells, B-cells
- Strongest increased analyte = TNFSF14
 - ⇒ 1.20-fold increase, uncorrected p-value=0.355
 - ⇒ T-cell proliferation

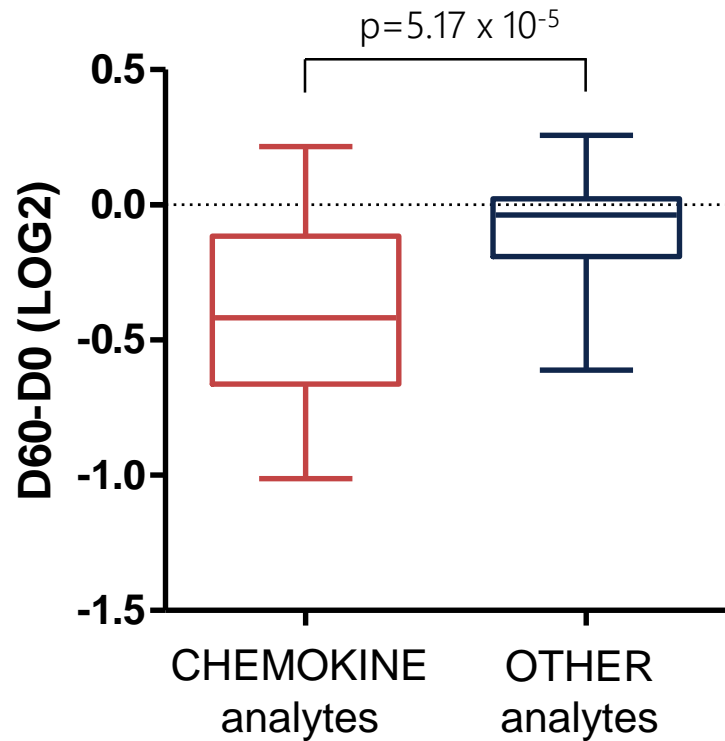


Change from baseline of 92 INFLAMMATORY analytes (Average of 6 patients)

Most prominent decrease observed in
CHEMOKINE family analytes



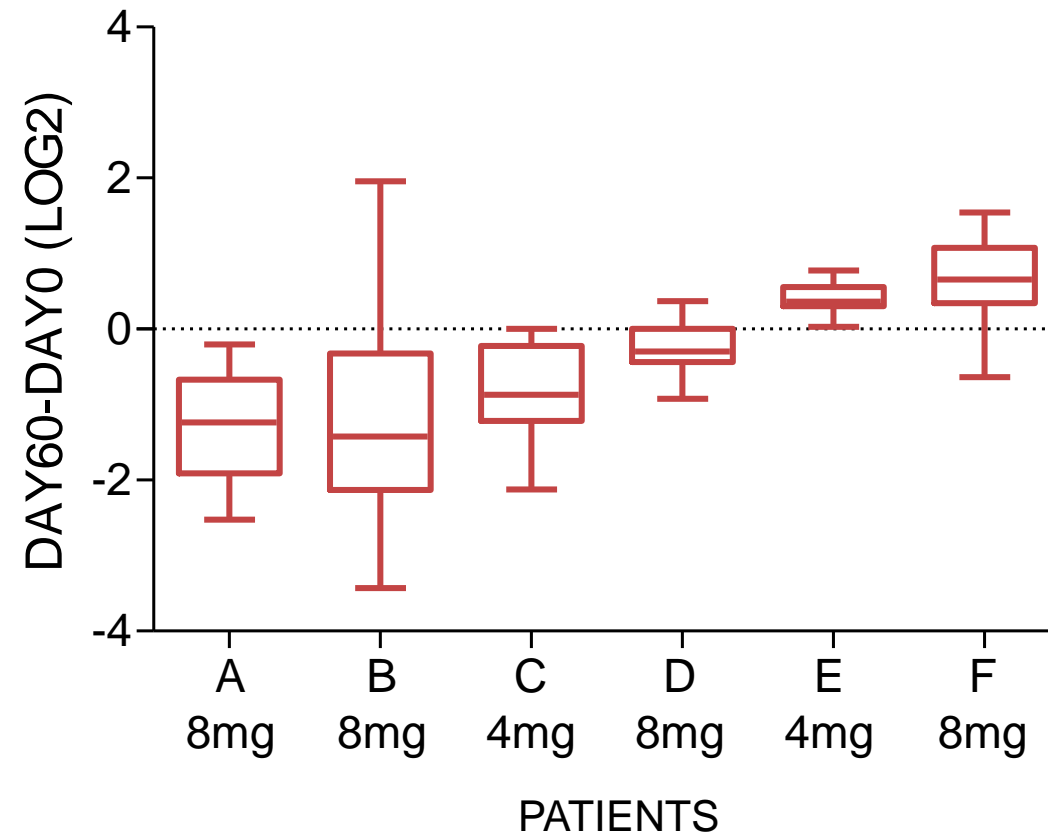
CHEMOKINE family analytes (Average of 6 patients)



Name	Mean log2 difference	P-value	-log10 P-value
CCL20	-1.012	0.056	1.255
CCL19	-1.002	0.182	0.740
CXCL10	-0.845	0.263	0.580
CCL23	-0.775	0.276	0.559
CXCL1	-0.626	0.363	0.441
CX3CL1	-0.582	0.109	0.963
MCP-2	-0.527	0.330	0.481
CCL11	-0.519	0.258	0.588
CXCL6	-0.424	0.502	0.299
CCL4	-0.411	0.242	0.615
CXCL5	-0.404	0.407	0.391
CCL25	-0.306	0.412	0.385
MCP-1	-0.306	0.255	0.594
CCL28	-0.143	0.392	0.407
CXCL11	-0.034	0.846	0.073
MCP-4	-0.015	0.854	0.069
CCL3	0.095	0.848	0.072
CXCL9	0.215	0.532	0.274

Observed decrease in inflammatory proteins is mainly driven by CHEMOKINE analytes.

CHEMOKINE family analytes in individual patients



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CONCLUSIONS

- Broad multiplex profiling of aqueous humor was found to be feasible using both OLINK (and AYOXXA) technologies, yielding information on >100 analytes from as little as 10 μ L ocular fluid. Data from both methods correlated well.
- In a cohort of 6 treatment-naïve DME patients, we observed an overall decrease of inflammatory proteins in aqueous humor samples taken after two injections of the anti-PIGF THR-317. Main contributor was a decrease in CHEMOKINE family proteins.
- LIMITATIONS: Limited sample number (N=6)
 - ⇒ Additional datasets will be required to confirm the observations made in this study and to correlate with clinical outcomes.

THANK YOU