Supplementary Table 1. DZB kinase profile and comparison with other FGFR-inhibitors in clinical development

Compound	Parameter	FGFR1	FGFR2	FGFR3	FGFR4	CSF1R	FGFR2 ratio
Derazantinib	mean IC50 (nM):	22.2	5.8	22.8	402	17.4	**1.0**
	Ratio to FGFR2:	**4**	**1**	**4**	**77**	**3**	
Erdafitinib	mean IC50 (nM):	4.1	2	3.1	26.7	190	**2.9**
	Ratio to FGFR2:	**2**	**1**	**2**	**13**	**95**	
Pemigatinib	mean IC50 (nM):	3.3	1.3	5.2	50.3	300	**4.5**
	Ratio to FGFR2:	**3**	**1**	**4**	39	**231**	
Infigratinib	mean IC50 (nM):	4.5	3	5.6	142	258	**1.9**
	Ratio to FGFR2:	**2**	**1**	**2**	**47**	**86**	
Rogaratinib	mean IC50 (nM):	7.5	1.4	8.8	25.6	162	**4.1**
	Ratio to FGFR2:	**5**	**1**	**6**	**18**	**116**	

The radiometric kinase assay was performed by the Contract Research Organization, Reaction Biology (Freiburg, Germany) using 10 different concentrations for each compound and kinase to determine the IC50. Results show the mean IC50 from duplicate assay-runs for the kinases shown, as well as the potency with respect to the most sensitive kinase (FGFR2) as a ratio, and a comparison of the potency of the different kinases based on the respective IC50 for FGFR2.

Supplementary Table 2. Inhibition of WT FGFR2 and FGFR-mutants in HeLa cells upon treatment with DZB and other FGFR-inhibitors.

		High Prevalence			Clinical Trial			Acquired resistance		
	WT	A97T	P253R	S252W	Y375C	F276C	C382R	V564F	N549K	K641R
DZB	107	127	191	295	124	104	161	>1000	>1000	>1000
Erdafitinib	2.5	2.1	2	2.1	0.4	1.2	1.3	>300	28.4	30.4
Pemigatinib	5.2	2	4	4.3	7.6	2.7	5.4	>300	>300	68.9
Infigratinib	5.5	7.8	4	7.1	9.5	6.2	6.2	>300	89.5	39.5
Rogaratinib	24	11.6	17.5	8.9	17	10.7	35	>300	>300	>300

Results show the IC50 for FGFR2 inhibition for DZB and 4 other FGRi. For DZB, 5 different concentrations were used and for the other compounds, 6 different concentrations were used for each HeLa cell line model.

Supplementary Table 3. Efficacy and tolerability of DZB, erdafitinib or pemigatinib in murine syngeneic tumors.

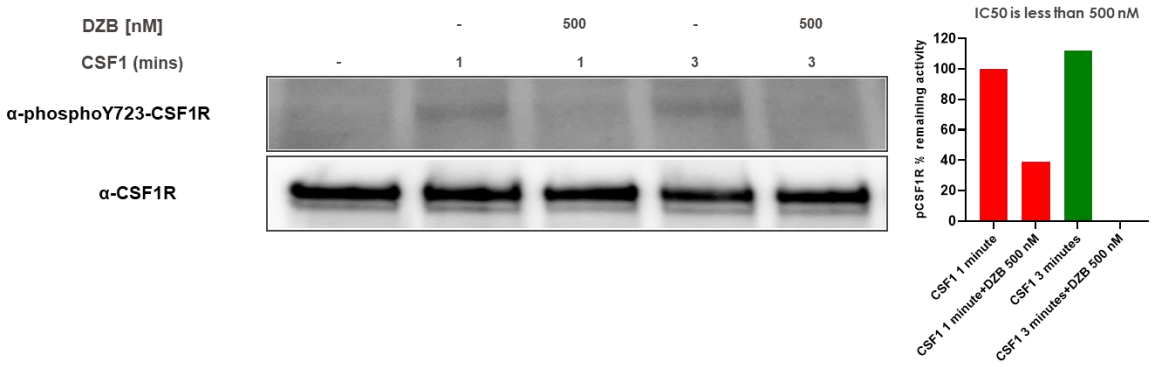
		RNA-Seq expression			FGFR	Efficacy: ΔT/C-TVol			Tolerability: ΔT/C-BW			Endpoint
Model	Histotype	FGFR1	FGFR2	FGFR3	Mutn/Fusion	DZB	Erdafitinib	Pemigatinib	DZB	Erdafitinib	Pemigatinib	Day
MB49	Bladder	2.5	-1.4	0.9		1.03	nd	nd	0.98	nd	nd	12
MBT-2	Bladder	5.8	-1.9	1.7		1.00	nd	nd	1.01	nd	nd	7
mBL6078	Bladder	7.6	0.5	-1.7		0.91	nd	nd	1.02	nd	nd	14
EMT6	Breast	7.0	-1.1	1.4		0.71	nd	nd	0.99	nd	nd	12
4T1	Breast	5.2	5.1	1.1		0.13	-0.03	0.09	0.94	0.94	0.96	21
JC	Breast	8.0	-1.2	-1.1	R1-CNN2	1.09	1.45	1.01	1.00	1.04	1.02	16
MC-38	CRC	6.7	2.0	0.5	R3:C478F	0.98	1.44	1.08	0.97	1.07	1.01	10
Colon-26	CRC	7.2	-2.0	-1.0	R1:S120F	0.98	0.97	0.82	0.93	0.85	0.96	10
KLN205	Lung	6.1	3.1	1.9		1.14	1.53	0.66	1.03	1.00	1.03	21
LLC	Lung	7.6	2.2	0.6	R1-EEF1A7	0.62	1.11	0.81	0.95	1.03	0.94	18
					Median:	0.98	1.28	0.82	0.99	1.02	0.99	

The 10 different tumor models were set-up as described in Methods, and all were grown s.c. except for the 4T1 cells which were injected in the mammary fat pad. Crown Biosciene provided the genetic information for FGFR, and there was none available for CSF1R. When tumor volumes reached a mean maximum of 100 mm^3, the mice were treated daily, by gavage with DZB (75 mg/kg), or erdafitinib (30 mg/kg) or pemigatinib (1 mg/kg) until the vehicle tumors reached the point where culling of the mice was required (TVol≥1500 mm^3). Results show the mean ΔT/C in each experiment at the respective endpoint, and the median efficacy and tolerability for the three different FGFRi.

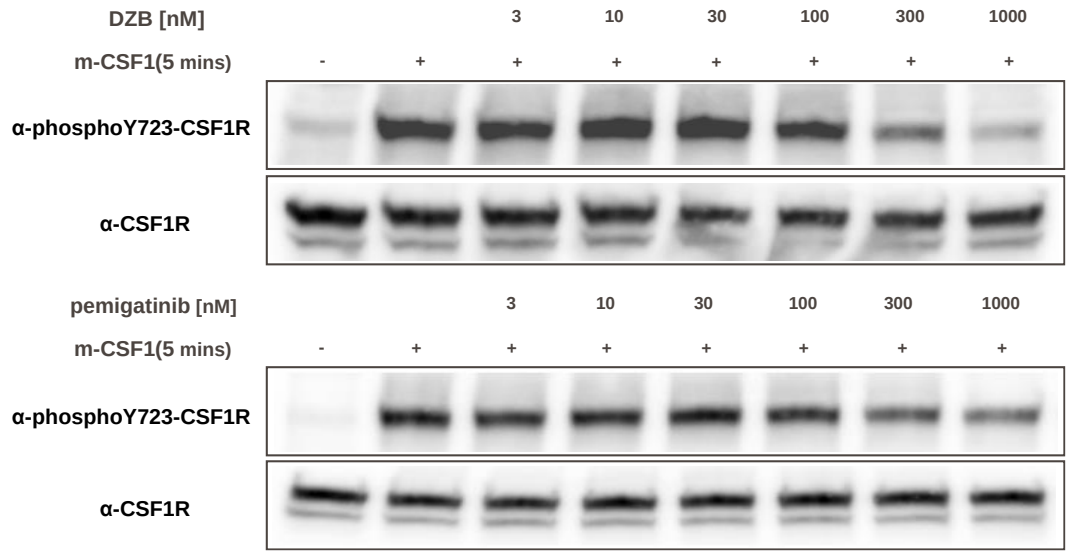
Supplementary Figure 1. Effect of derazantinib on CSF1R in the GDM-1 human myelomonoblastic leukemia cell line (A) and RAW264.7 cell line (B).

Western-blot analysis of GDM-1 cells (A) and RAW264.7 cells (B) pre-treated with DZB at the concentration indicated for 1 hour and stimulated with m-CSF ligand for 1 or 3 minutes. Specific p-CSF1R and total CSF1R antibodies were used.

A. GDM-1

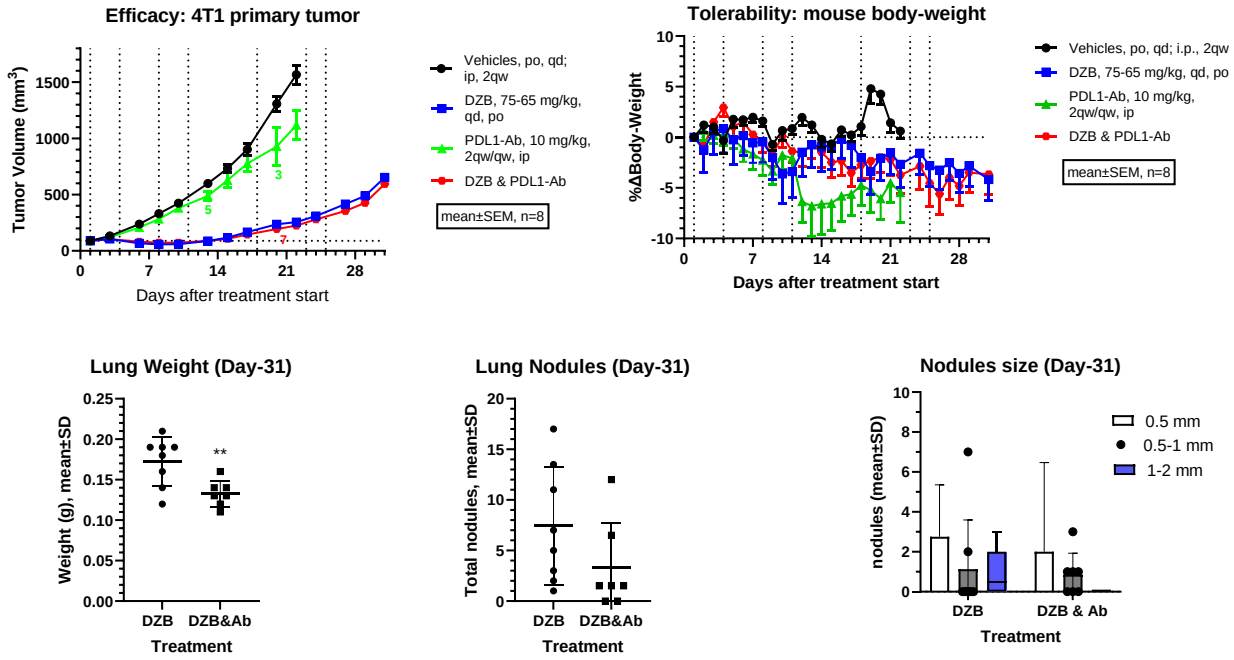


B. RAW264.7



Supplementary Figure 2. Efficacy of DZB alone and in combination with the murine PDL1-Ab against 4T1 primary tumors and lung metastases.

Murine 4T1 cells were injected into the mammary fat pad and treatment began as shown when the tumors reached 100 mm^3. Results show the mean±SEM (n=8) for tumor volume and the percentage body-weight change. The DZB monotherapy group and the combination group were treated until day-31 when mice were culled, the lungs ablated and weighed and the numbers of nodules counted and sizes estimated. For the lung-weight and nodules, a non-paired, parametric 2-tailed t-test was applied, where **p=0.008 (weight) and p=0.089 (nodules).



Supplementary Figure 3. Examples of IHC staining for $CD4^+$ and $CD8^+$ cells in tumor slices from the 4T1 model PD-experiment.

Representative images (40-fold magnification) by Multiplex IF assay of tumor slices (4 μm) for the 4 different treatment groups (data in Figure 6).