

Supplementary Table S1. Characteristics of the study population.

Characteristic	Institution			Total
	DF/BWCC	URMC	SCI	
Number of subjects	109	73	123	305
Men (n, %)	47 (43%)	44 (60%)	76 (62%)	167 (55%)
Age, (median, IQR), years	64 (58-71)	67 (59-72)	69 (62-75)	67 (59-73)
Race				
White	82 (75%)	65 (89%)	93 (76%)	240 (79%)
Black	1 (1%)	3 (4%)	1 (1%)	5 (2%)
Asian	1 (1%)	2 (3%)	23 (19%)	26 (8%)
Other/Unknown	25 (23%)	3 (4%)	6 (4%)	34 (11%)
pT stage (n, %)				
T1-T2	8 (7%)	4 (5%)	39 (32%)	51 (17%)
T3-T4	101 (93%)	69 (95%)	83 (67%)	253 (83%)
Tx	0	0	1 (1%)	1 (<1%)
pN stage (n, %)				
N0	34 (31%)	18 (25%)	42 (34%)	94 (31%)
N1	75 (69%)	55 (75%)	81 (66%)	211 (69%)
Tumor grade (n, %)				
Well/Moderately differentiated	56 (51%)	39 (53%)	82 (67%)	177 (58%)
Poorly differentiated/ Undifferentiated	51 (47%)	32 (44%)	38 (31%)	121 (40%)
Unknown	2 (2%)	2 (3%)	3 (2%)	7 (2%)
Lymphovascular invasion (n, %)				
Negative	48 (44%)	25 (34%)	60 (49%)	133 (44%)
Positive	52 (48%)	47 (64%)	42 (34%)	141 (46%)
Unknown	9 (8%)	1 (1%)	21 (17%)	31 (10%)
Resection margin status (n, %)				
R0	42 (38%)	40 (55%)	69 (56%)	151 (50%)
R1	65 (60%)	33 (45%)	51 (41%)	149 (49%)
R2	2 (2%)	0	2 (2%)	4 (1%)
Rx (not evaluable)	0	0	1 (1%)	1 (<1%)
Adjuvant systemic chemotherapy (n, %)				
No	29 (26%)	20 (27.5%)	37 (30%)	86 (28%)
Yes	76 (70%)	50 (68.5%)	67 (54.5%)	193 (63%)
Unknown	4 (4%)	3 (4%)	19 (15.5%)	26 (9%)
Adjuvant radiation therapy (n, %)				
No	45 (41%)	43 (59%)	68 (55%)	156 (51%)
Yes	60 (55%)	27 (37%)	36 (29%)	123 (40%)
Unknown	4 (4%)	3 (4%)	19 (16%)	26 (9%)

Abbreviations: DF/BWCC: Dana-Farber/Brigham and Women's Cancer Center; SCI: Stanford Cancer Institute; URMC: University of Rochester Medical Center

Supplementary Table S2. List of antibodies and fluorophores used in the multiplex immunofluorescence staining procedures.

Panel	Marker	Clone	Manufacturer, catalog number	Antibody dilution	Fluorophore	Fluorophore dilution	Antigen retrieval before the primary antibody
Myeloid	CD15	Carb-3	DAKO, M3631	1:200	Opal 520	1:100	Tris-EDTA
Myeloid	CD14	SP192	Abcam, ab183322	1:300	Opal 570	1:300	ER1
Myeloid	ARG1	EPR6672	Abcam, ab133543	1:500	Opal 690	1:150	ER1
Myeloid	HLA-DR	TAL1B5	Santa Cruz, sc-53319	1:1000	Opal 540	1:200	ER1
Myeloid	CD33	PWS44	Leica Biosystems, NCL-L-CD33	1:75	Opal 650	1:400	ER1
Myeloid	CK	AE1/AE3; C11	DAKO, M3515; Cell Signaling Technology, #4545	1:50; 1:500	Opal 620	1:500	ER1
Macrophage	IRF5	EPR17067	Abcam, ab181553	1:4000	Opal 650	1:300	Tris-EDTA
Macrophage	CD163	10D6	Leica Biosystems, 2021-08	1:400	Opal 570	1:300	ER1
Macrophage	CD68	PG-M1	DAKO, M0876	1:25	Opal 520	1:100	ER1
Macrophage	CD86	E2G8P	Cell Signaling Technology, #91882	1:50	Opal 540	1:200	ER2
Macrophage	MRC1	E2L9N	Cell Signaling Technology, #91992	1:600	Opal 690	1:150	ER1
Macrophage	CK	See above	See above	1:50; 1:500	Opal 620	1:500	ER1

Abbreviations: ER1/2: BOND Epitope Retrieval Solution 1/2 (Leica Biosystems, Buffalo, IL, USA)

Supplementary Table S3. List of reagents and equipment used in multiplex immunofluorescence.

Reagent	Manufacturer, catalog number
Xylene	Fisher Scientific (Pittsburgh, PA, USA), X3P1GAL
Ethanol	Fisher Scientific, HC-800-1GAL
Tris-EDTA (pH 9.0)	DAKO (Copenhagen, Denmark), S1699
BOND Epitope Retrieval Solution 1	Leica Biosystems (Buffalo, IL, USA), AR9961
BOND Epitope Retrieval Solution 2	Leica Biosystems, AR9640
Protein Block, Serum-Free	DAKO, X0909
Opal polymer HRP Ms + Rb	Akoya Biosciences (Hopkinton, MA, USA), ARH1001EA
Spectral DAPI	Akoya Biosciences, FP1490
ProLong Diamond Antifade Mountant	Fisher Scientific, P36970
FF Cover Glass	Fisher Scientific, 125485M
Equipment	
2100-Retriever	Electron Microscopy Sciences (Hatfield, PA, USA), 62700-10
Leica BOND RX Research Stainer	Leica Biosystems

Supplementary Table S4. Myeloid immune cell densities within intraepithelial, stromal, and whole tissue areas.

Myeloid immune cell subset	Myeloid immune cell densities (cells/mm ²)		
	Intraepithelial, median (IQR)	Stromal, median (IQR)	Whole tissue area, median (IQR)
CD15⁺ cells	83.2 (19.1-210.9)	100.2 (28.4-422.8)	93.9 (27.6-353.6)
CD15⁺ARG1⁺	46.3 (7.4-139.2)	64.3 (15.7-271.1)	62.6 (15.9-222.3)
CD15 ⁺ ARG1 ⁺ CD33 ⁺	0.6 (0.0-12.3)	1.8 (0.0-8.6)	2.0 (0.0-9.7)
CD15 ⁺ ARG1 ⁺ CD33 ⁻	35.2 (6.1-124.3)	58.8 (13.7-260.0)	54.0 (14.0-212.7)
CD15⁺ARG1⁻	18.2 (5.0-62.9)	28.5 (8.2-93.2)	24.8 (8.3-81.3)
CD15 ⁺ ARG1 ⁻ CD33 ⁺	0 (0.0-2.9)	0.2 (0.0-2.4)	0.5 (0.0-2.8)
CD15 ⁺ ARG1 ⁻ CD33 ⁻	17.4 (4.1-56.1)	26.6 (7.4-92.2)	23.7 (7.9-80.8)
CD14⁺ cells	101.3 (43.9-254.9)	391.5 (206.5-615.1)	330.1 (172.4-521.2)
CD14⁺ARG1⁺	0 (0.0-7.0)	3.6 (0.6-15.8)	3.1 (0.5-12.9)
CD14 ⁺ ARG1 ⁺ HLA-DR ⁺ CD33 ⁺	0 (0.0-0.0)	0 (0.0-1.6)	0 (0.0-1.5)
CD14 ⁺ ARG1 ⁺ HLA-DR ⁺ CD33 ⁻	0 (0.0-0.0)	1.1 (0.0-5.6)	0.9 (0.0-4.2)
CD14 ⁺ ARG1 ⁺ HLA-DR ⁻ CD33 ⁺	0 (0.0 0.0)	0.0 (0.0-1.4)	0 (0.0-1.6)
CD14 ⁺ ARG1 ⁺ HLA-DR ⁻ CD33 ⁻	0 (0.0 - 1.7)	1.0 (0.0 - 5.3)	0.9 (0.0 - 4.4)
CD14⁺ARG1⁻	99.6 (42.1-229.4)	364.5 (199.5-582.7)	315.6 (168.5-499.2)
CD14 ⁺ ARG1 ⁻ HLA-DR ⁺ CD33 ⁺	2.5 (0.0-13.2)	15.0 (3.8-34.9)	12.2 (3.4-34.1)
CD14 ⁺ ARG1 ⁻ HLA-DR ⁺ CD33 ⁻	17.4 (5.4-40.5)	177.33 (88.9-279.1)	138.9 (72.1-236.1)
CD14 ⁺ ARG1 ⁻ HLA-DR ⁻ CD33 ⁺	7.8 (0.0-30.9)	12.3 (3.9-28.8)	12.1 (4.1-28.8)
CD14 ⁺ ARG1 ⁻ HLA-DR ⁻ CD33 ⁻	48.7 (17.5-124.7)	127.4 (65.4-212.6)	109.8 (55.8-201.4)
Overall macrophages	153.7 (74.4-289.0)	871.0 (528.5-1375.6)	680.8 (418.5-1015.8)
M1-polarized macrophages^a	39.3 (16.5-82.2)	176.8 (101.1-353.8)	142.5 (81.9-261.8)
M2-polarized macrophages^a	24.1 (6.2-72.6)	177.1 (92.3-323.6)	145.1 (68.2-265.4)

^aM1-polarized macrophages were defined as macrophages in the 4th quartile and M2-polarized macrophages as macrophages in the 1st quartile of M1-M2 index distribution. Abbreviations: IQR:interquartile range

Supplementary Table S5. Macrophage densities and tumor nodal metastases.

Macrophage subset ^a	Nodal metastases		
	N0 (n=90)	N1 (n=206)	P ^c
Overall macrophages, median (IQR)	576 (353-868)	727 (436-1040)	0.02
M1-polarized, median (IQR)	127 (61-207)	150 (89-292)	0.01
M2-polarized, Median (IQR)	153 (79-241)	144 (67-270)	0.99

^aThe densities of macrophages are based on the overall cell densities (intraepithelial+stromal areas). M1-polarized macrophages were defined as macrophages in the 4th quartile and M2-polarized macrophages as macrophages in the 1st quartile of M1-M2-index distribution.

^b P value calculated with Wilcoxon rank-sum test.

Supplementary Table S6. Myeloid immune cell densities and tumor molecular characteristics.

Myeloid immune cell subset ^a	<i>KRAS</i> ^b			<i>CDKN2A</i> ^b			<i>SMAD4</i> ^b			<i>TP53</i> ^b		
	Wild-type (n=23)	Mutant (n=269)	<i>P</i> ^c	Intact (n=99)	Lost (n=193)	<i>P</i> ^c	Intact (n=146)	Lost (n=146)	<i>P</i> ^c	Wild-type (n=105)	Altered (n=187)	<i>P</i> ^c
CD15⁺ , median (IQR)	266 (15-600)	94 (28-333)	0.68	106 (30-359)	94 (27-364)	0.94	91 (32-330)	97 (26-399)	0.95	75 (20-267)	122 (33-402)	0.04
CD15⁺ARG1⁺ , median (IQR)	81 (7.2-178)	63 (16-229)	0.83	66 (20-199)	63 (15-239)	0.93	65 (20-194)	61 (15-292)	0.82	47 (13-177)	71 (19-276)	0.06
CD15⁺ARG1⁻ , median (IQR)	63 (7.8-175)	25 (8.3-77)	0.25	25 (8.2-88)	26 (8.5-77)	0.70	25 (8.3-81)	27 (8.3-82)	0.73	22 (6.6-56)	29 (10-96)	0.03
CD14⁺ , median (IQR)	479 (214-781)	328 (171-513)	0.08	317 (159-513)	331 (183-523)	0.43	365 (209-553)	286 (158-513)	0.04	319 (180-544)	343 (172-516)	0.73
CD14⁺ARG1⁺ , median (IQR)	5.1 (1.0-31)	3.0 (0.5-11)	0.61	3.7 (1.0-11)	2.5 (0.5-13)	0.63	3.9 (1.0-14.2)	2.1 (0.4-9.6)	0.08	2.3 (0.5-9.7)	3.6 (0.5-16)	0.09
CD14⁺ARG1⁻ , median (IQR)	441 (212-666)	315 (169-486)	0.10	292 (158-511)	318 (181-499)	0.47	354 (184-536)	266 (156-465)	0.03	311 (174-525)	319 (170-494)	0.90
Overall macrophages , median (IQR)	799 (341-913)	680 (424-1030)	0.88	686 (462-1017)	682 (405-1030)	0.49	652 (419-914)	714 (422-1135)	0.35	635 (383-873)	723 (458-1142)	0.04
M1-polarized , median (IQR)	218 (94-442)	143 (81-262)	0.10	145 (93-299)	149 (80-263)	0.48	145 (85-278)	148 (82-261)	0.73	146 (85-252)	146 (82-278)	0.78
M2-polarized , median (IQR)	120 (26-280)	146 (63-265)	0.47	137 (59-257)	149 (61-268)	0.71	143 (64-237)	146 (58-275)	0.57	121 (51-249)	148 (74-269)	0.16

^aThe densities of myeloid immune cell subsets are based on the overall cell densities (intraepithelial + stromal areas). M1-polarized macrophages were defined as macrophages in the 4th quartile and M2-polarized macrophages as macrophages in the 1st quartile of the M1-M2-index distribution.

^bThe status of *KRAS*, *CDKN2A*, *SMAD4* and *TP53* was determined using a combination of pyrosequencing and next generation sequencing for *KRAS* and immunohistochemistry (IHC) and next generation sequencing for *CDKN2A*, *SMAD4* and *TP53*, as previously described (Qian et al., 2018).

^c*P* value calculated with Wilcoxon rank-sum test.

Abbreviations: IQR:interquartile range

Supplementary Table S7. Univariable and multivariable Cox regression models for overall survival according to ARG1⁺ and ARG1⁻ granulocytic (CD15⁺) and monocytic (CD14⁺) cells.

Myeloid immune cell subset ^a	No. of patients	Median, IQR (cells/mm ²)	Median survival (months)	Univariable HR (95% CI)	Multivariable HR (95% CI) ^b
CD15⁺ARG1⁺					
Q1	72	6.6 (3.2-9.9)	26.7	1.00 (reference)	1.00 (reference)
Q2	73	27.5 (22.8-38.3)	21.0	1.30 (0.89-1.90)	1.05 (0.71-1.57)
Q3	73	119.2 (79.6-164.4)	16.7	1.62 (1.10-2.37)	1.24 (0.83-1.84)
Q4	72	555.2 (342.9-767.9)	16.9	1.55 (1.06-2.27)	1.25 (0.83-1.87)
<i>P</i> _{trend}				0.096	0.317
CD15⁺ARG1⁻					
Q1	72	3.3 (1.5-6.4)	24.4	1.00 (reference)	1.00 (reference)
Q2	73	14.9 (11.6-20.2)	19.1	1.49 (1.02-2.17)	1.32 (0.89-1.95)
Q3	73	49.4 (36.8-64.8)	18.2	1.32 (0.91-1.93)	1.17 (0.78-1.76)
Q4	72	168.2 (126.8-219.6)	20.3	1.24 (0.85-1.82)	1.08 (0.72-1.60)
<i>P</i> _{trend}				0.808	0.716
CD14⁺ARG1⁺					
Q1	115	0.0 (0.0-0.0)	22.4	1.00 (reference)	1.00 (reference)
Q2	58	3.1 (2.2-3.9)	20.7	1.16 (0.82-1.65)	1.14 (0.79-1.63)
Q3	59	8.8 (5.7-14.2)	18.2	1.19 (0.83-1.72)	1.04 (0.71-1.54)
Q4	58	34.7 (21.1-78.0)	18.2	1.24 (0.86-1.78)	1.05 (0.71-1.55)
<i>P</i> _{trend}				0.209	0.824
CD14⁺ARG1⁻					
Q1	72	108.7 (69.7-141.4)	16.6	1.00 (reference)	1.00 (reference)
Q2	73	228.4 (193.0-286.4)	18.1	1.13 (0.79-1.62)	1.03 (0.70-1.52)
Q3	73	416.5 (339.5-459.7)	27.4	0.66 (0.45-0.96)	0.65 (0.43-0.97)
Q4	72	661.6 (586.7-864.9)	17.7	1.12 (0.77-1.62)	1.04 (0.70-1.54)
<i>P</i> _{trend}				0.634	0.508

^aThe densities of myeloid immune cell subsets are based on the overall densities in tumor area (intraepithelial + stromal).

^bCox proportional hazards regression model adjusted for age, sex, pathologic N stage (N0, N1, Nx), tumor grade (well/moderately differentiated, poorly differentiated, unknown), lymphovascular invasion (negative, positive, unknown), resection margin status (R0, R1, R2, unknown), receipt of adjuvant treatment. Overall survival: n=290.

Abbreviations: CI:confidence interval; HR:hazard ratio; IQR:interquartile range; Q:quartile

Supplementary Table S8. Univariable and multivariable Cox regression models for disease-free and overall survival according to stromal and intraepithelial ARG1⁺ granulocytic (CD15⁺) cells.

Myeloid immune cell subset	Disease-free survival					Overall survival				
	No. of patients	Median, IQR (cells/mm ²)	Median survival (months)	Univariate HR (95% CI)	Multivariable HR (95% CI) ^a	No. of patients	Median, IQR (cells/mm ²)	Median survival (months)	Univariate HR (95% CI)	Multivariable HR (95% CI) ^a
Stromal region										
CD15⁺ARG1⁺										
Q1	72	6.6 (3.8-10.7)	17.1	1.00 (reference)	1.00 (reference)	72	6.6 (3.8-10.7)	29.4	1.00 (reference)	1.00 (reference)
Q2	71	29.1(20.8-44.3)	13.4	1.33 (0.89-2.00)	1.12 (0.73-1.73)	73	30.7 (21.1-44.3)	20.7	1.44 (0.99-2.11)	1.04 (0.70-1.55)
Q3	73	123.3 (82.0-180.7)	10.1	1.84 (1.25-2.73)	1.37 (0.90-2.09)	73	123.3 (82.0-180.7)	17.4	1.65 (1.12-2.42)	1.13 (0.75-1.69)
Q4	70	653.4 (419.8-1066.6)	9.9	1.83 (1.23-2.72)	1.95 (1.25-3.02)	72	653.4 (420.9-1055.9)	16.9	1.65 (1.12-2.42)	1.23 (0.81-1.86)
<i>P_{trend}</i>				0.015	0.002				0.080	0.313
Intraepithelial region										
CD15⁺ARG1⁺										
Q1	71	0 (0-2.6)	14.4	1.00 (reference)	1.00 (reference)	72	0 (0-3.0)	24.2	1.00 (reference)	1.00 (reference)
Q2	72	20.2 (11.4-29.7)	11.1	1.09 (0.73-1.63)	0.93 (0.62-1.40)	73	20.2 (11.5-30.0)	18.5	1.12 (0.77-1.63)	1.02 (0.69-1.51)
Q3	73	81.7 (53.9-106.8)	13.9	1.03 (0.70-1.53)	1.00 (0.67-1.50)	73	81.7 (53.9-106.8)	20.3	1.02 (0.70-1.48)	0.97 (0.66-1.44)
Q4	70	284.6 (208.7-446.7)	10.3	1.54 (1.05-2.27)	1.37 (0.92-2.05)	72	287.9 (209.3-457.2)	16.9	1.38 (0.95-2.00)	1.14 (0.77-1.69)
<i>P_{trend}</i>				0.017	0.074				0.092	0.458

^aCox proportional hazards regression model adjusted for age, sex, pathologic N stage (N0, N1, Nx), tumor grade (well/moderately differentiated, poorly differentiated, unknown), lymphovascular invasion (negative, positive, unknown), resection margin status (R0, R1, R2, unknown), receipt of adjuvant treatment. Disease-free survival: n=286; overall survival: n=290.

Abbreviations: CI:confidence interval; HR:hazard ratio; IQR:interquartile range; Q:quartile

Supplementary Table S9. Univariable and multivariable Cox regression models for disease-free and overall survival according to CD14⁺HLA-DR⁺CD33⁻ and CD14⁺HLA-DR⁻CD33⁻ cells.

Myeloid immune cell subset	Disease-free survival					Overall survival				
	No. of patients	Median, IQR (cells/mm ²)	Median survival (months)	Univariate HR (95% CI)	Multivariable HR (95% CI) ^a	No. of patients	Median, IQR (cells/mm ²)	Median survival (months)	Univariate HR (95% CI)	Multivariable HR (95% CI) ^a
CD14⁺HLA-DR⁺CD33⁻										
Q1	70	38.4 (24.6-61.6)	11.1	1.00 (reference)	1.00 (reference)	72	38.4 (24.6-62.3)	16.3	1.00 (reference)	1.00 (reference)
Q2	72	111.7 (88.8-127.7)	10.1	1.08 (0.73-1.60)	1.33 (0.88-1.99)	73	111.6 (88.4-126.7)	16.9	1.08 (0.75-1.54)	1.43 (0.97-2.12)
Q3	73	185.4 (162.5-215.9)	16.5	0.61 (0.41-0.90)	0.73 (0.47-1.13)	73	185.4 (162.5-215.9)	30.2	0.64 (0.44-0.93)	0.66 (0.44-0.98)
Q4	71	333.8 (282.4-448.2)	13.3	0.80 (0.55-1.17)	0.77 (0.52-1.14)	72	330.3 (285.0-444.9)	20.7	0.76 (0.52-1.10)	0.77 (0.52-1.15)
<i>P_{trend}</i>				0.051	0.048				0.024	0.020
CD14⁺HLA-DR⁻CD33⁻										
Q1	70	36.8 (25.4-51.2)	12.3	1.00 (reference)	1.00 (reference)	72	37.2 (26.4-51.2)	18.1	1.00 (reference)	1.00 (reference)
Q2	72	80.2 (64-97.5)	14.4	0.88 (0.59-1.31)	0.90 (0.60-1.36)	73	81 (64.4-97.6)	24.6	0.98 (0.68-1.42)	1.01 (0.69-1.48)
Q3	73	149.2 (121.1-177.2)	11.6	1.00 (0.68-1.48)	1.00 (0.66-1.51)	73	149.2 (121.1-177.2)	20.5	1.01 (0.69-1.50)	0.97 (0.64-1.45)
Q4	71	328.8 (220.5-438.9)	10.5	1.13 (0.77-1.66)	1.02 (0.68-1.54)	72	330.8 (221.9-440.4)	18.2	1.17 (0.81-1.70)	1.17 (0.79-1.74)
<i>P_{trend}</i>				0.424	0.800				0.394	0.493

^aCox proportional hazards regression model adjusted for age, sex, pathologic N stage (N0, N1, Nx), tumor grade (well/moderately differentiated, poorly differentiated, unknown), lymphovascular invasion (negative, positive, unknown), resection margin status (R0, R1, R2, unknown), receipt of adjuvant treatment. Disease-free survival: n=286; overall survival: n=290.

Abbreviations: CI:confidence interval; HR:hazard ratio; IQR:interquartile range; Q:quartile

Supplementary Table S10. Univariable and multivariable Cox regression models for disease-free and overall survival according to overall macrophage population.

Myeloid immune cell subset	Disease-free survival					Overall survival				
	No. of patients	Median, IQR (cells/mm ²)	Median survival (months)	Univariate HR (95% CI)	Multivariable HR (95% CI) ^a	No. of patients	Median, IQR (cells/mm ²)	Median survival (months)	Univariate HR (95% CI)	Multivariable HR (95% CI) ^a
Overall region										
Macrophage density										
Q1	69	296.0 (260.3-363.2)	14.1	1.00 (reference)	1.00 (reference)	72	299.4 (259.6-363.7)	20.9	1.00 (reference)	1.00 (reference)
Q2	75	548.0 (482.3-606.1)	14.4	0.76 (0.50-1.14)	0.87 (0.57-1.32)	75	548.0 (482.3-606.1)	25.9	0.67 (0.46-0.97)	0.70 (0.47-1.05)
Q3	75	808.9 (738.5-913.8)	14.1	1.11 (0.75-1.65)	0.92 (0.61-1.39)	75	808.9 (738.5-913.8)	20.0	1.03 (0.72-1.48)	0.90 (0.62-1.31)
Q4	73	1349.8 (1193.0-1685.3)	9.4	1.32 (0.89-1.95)	1.21 (0.80-1.82)	74	1351.5 (1193.0-1726.9)	17.8	1.17 (0.81-1.68)	0.93 (0.64-1.37)
<i>P_{trend}</i>				0.044	0.212				0.088	0.846
Stromal region										
Macrophage density										
Q1	70	382.8 (313.9-437.2)	13.7	1.00 (reference)	1.00 (reference)	72	382.8 (307.5-437.1)	22.4	1.00 (reference)	1.00 (reference)
Q2	74	693.8 (599.4-773.3)	15.9	0.81 (0.54-1.23)	0.72 (0.47-1.09)	75	691.2 (598.1-773.3)	24.4	0.89 (0.61-1.30)	0.79 (0.53-1.17)
Q3	75	1038.6 (953.9-1226.8)	10.6	1.17 (0.80-1.73)	1.18 (0.78-1.78)	75	1038.6(953.9-1226.8)	20.6	1.12 (0.78-1.62)	1.03 (0.70-1.51)
Q4	73	1758.9 (1550-2180.9)	9.9	1.32 (0.89-1.95)	1.19 (0.79-1.81)	74	1760.9 (1550-2180.9)	16.8	1.32 (0.92-1.90)	1.04 (0.71-1.53)
<i>P_{trend}</i>				0.041	0.084				0.054	0.467
Intraepithelial region										
Macrophage density										
Q1	71	44.1 (26.8-60.8)	15.9	1.00 (reference)	1.00 (reference)	73	44.4 (27-61.3)	26.0	1.00 (reference)	1.00 (reference)
Q2	75	111.5 (90.2-143)	9.8	1.63 (1.10-2.43)	1.92 (1.27-2.88)	75	111.5 (90.2-143)	19.1	1.64 (1.13-2.37)	1.69 (1.15-2.49)
Q3	75	211.8 (180.9-264)	11.5	1.40 (0.95-2.07)	1.69 (1.12-2.55)	75	211.8 (180.9-264)	20.5	1.36 (0.93-1.99)	1.61 (1.08-2.40)
Q4	71	494.4 (375.7-643.6)	10.3	1.40 (0.94-2.08)	1.30 (0.86-1.96)	73	494.4 (378.6-619.5)	18.2	1.58 (1.09-2.29)	1.31 (0.88-1.94)
<i>P_{trend}</i>				0.345	0.835				0.092	0.656

^aCox proportional hazards regression model adjusted for age, sex, pathologic N stage (N0, N1, Nx), tumor grade (well/moderately differentiated, poorly differentiated, unknown), lymphovascular invasion (negative, positive, unknown), resection margin status (R0, R1, R2, unknown), receipt of adjuvant treatment. Disease-free survival: n=292; overall survival: n=296.

Abbreviations: CI, confidence interval; HR, hazard ratio; IQR, interquartile range; Q, quartile

Supplementary Table S11. Univariable and multivariable Cox regression models for disease-free and overall survival according to M1- and M2-polarized macrophage densities.

Myeloid immune cell subset ^a	Disease-free survival					Overall survival				
	No. of patients	Median, IQR (cells/mm ²)	Median survival (months)	Univariate HR (95% CI)	Multivariable HR (95% CI) ^b	No. of patients	Median, IQR (cells/mm ²)	Median survival (months)	Univariate HR (95% CI)	Multivariable HR (95% CI) ^b
Overall region										
M1-polarized macrophages										
Q1	69	47.8 (33.2-61.0)	14.2	1.00 (reference)	1.00 (reference)	72	47.9 (32.0-62.3)	21.3	1.00 (reference)	1.00 (reference)
Q2	75	109.3 (93.6-125.3)	11.6	1.04 (0.70-1.55)	0.86 (0.56-1.31)	75	109.3 (93.6-125.3)	20.0	1.25 (0.86-1.81)	0.99 (0.66-1.47)
Q3	75	184.1 (159.0-217.1)	14.4	0.99 (0.67-1.47)	1.02 (0.68-1.52)	75	184.1 (159.0-217.1)	20.1	1.09 (0.75-1.59)	1.03 (0.70-1.54)
Q4	73	378.7 (304.6-488.3)	10.5	1.05 (0.71-1.56)	0.76 (0.50-1.16)	74	374.0 (304.6-488.3)	20.5	1.12 (0.77-1.62)	0.87 (0.59-1.29)
<i>P_{trend}</i>				0.863	0.254				0.844	0.439
M2-polarized macrophages										
Q1	71	37.3 (20.9-51.3)	12.0	1.00 (reference)	1.00 (reference)	72	37.3 (21.6-51.6)	23.9	1.00 (reference)	1.00 (reference)
Q2	73	103.7 (83.9-119.5)	15.9	0.75 (0.50-1.11)	0.70 (0.46-1.06)	75	103.7 (83.9-120.2)	20.9	0.94 (0.65-1.35)	1.00 (0.68-1.48)
Q3	75	192.5 (167.1-225.5)	13.5	0.90 (0.61-1.32)	1.05 (0.71-1.56)	75	192.5 (167.1-225.5)	20.5	0.93 (0.64-1.34)	1.14 (0.78-1.68)
Q4	73	353.0 (297.9-479.3)	9.9	1.20 (0.84-1.76)	1.32 (0.90-1.94)	74	352.2 (297.9-479.3)	17.7	1.32 (0.92-1.89)	1.20 (0.83-1.74)
<i>P_{trend}</i>				0.149	0.035				0.097	0.268
Stromal region										
M1-polarized macrophages										
Q1	70	58.8 (35-74.8)	14.1	1.00 (reference)	1.00 (reference)	72	58.1 (34.6-73.9)	24.4	1.00 (reference)	1.00 (reference)
Q2	74	132.5 (113.7-153)	13.6	1.01 (0.67-1.50)	0.80 (0.52-1.21)	75	132 (113-153)	20.9	1.08 (0.74-1.56)	0.88 (0.59-1.31)
Q3	75	223.6 (200.3-292.4)	14.1	0.85 (0.57-1.28)	0.88 (0.58-1.33)	75	223.6 (200.3-292.4)	20.6	1.08 (0.74-1.57)	1.02 (0.69-1.52)
Q4	73	480.5 (433.4-621.7)	10.0	1.18 (0.80-1.73)	0.84 (0.56-1.27)	74	479.5 (432.3-621.7)	18.5	1.20 (0.83-1.73)	0.95 (0.65-1.41)
<i>P_{trend}</i>				0.321	0.675				0.340	0.980
M2-polarized macrophages										
Q1	71	51.4 (28.6-67.8)	11.5	1.00 (reference)	1.00 (reference)	72	51.2 (27.8-67.6)	23.9	1.00 (reference)	1.00 (reference)
Q2	74	138 (113-154.6)	15.5	0.70 (0.47-1.03)	0.70 (0.46-1.05)	75	138.7 (113-159.6)	22.1	0.84 (0.58-1.22)	0.89 (0.61-1.32)
Q3	74	238.3 (193-285.8)	14.2	0.86 (0.59-1.26)	0.93 (0.63-1.38)	75	237.5 (193-285.8)	20.6	0.91 (0.63-1.32)	1.10 (0.74-1.62)
Q4	73	473.6 (378.6-593.1)	9.7	1.24 (0.85-1.80)	1.31 (0.89-1.94)	74	464 (378.6-593.1)	17.7	1.42 (1.00-2.03)	1.25 (0.86-1.80)
<i>P_{trend}</i>				0.076	0.044				0.017	0.136
Intraepithelial region										

M1-polarized macrophages

Q1	71	9.2 (1.4-14.5)	14.3	1.00 (reference)	1.00 (reference)	72	8.8(1.9-14.3)	25.3	1.00 (reference)	1.00 (reference)
Q2	74	26.7 (19.4-34.7)	14.2	0.92 (0.62-1.37)	0.92 (0.61-1.38)	75	26.5(19.4-34.7)	20.6	1.27 (0.87-1.85)	1.23 (0.83-1.83)
Q3	73	53.4 (44.8-66.3)	9.6	1.32 (0.90-1.95)	1.21 (0.80-1.83)	75	54.1(44.8-67.6)	17.4	1.64 (1.13-2.39)	1.55 (1.04-2.31)
Q4	74	130.2 (108.4-188.4)	10.3	1.11 (0.76-1.63)	1.03 (0.69-1.54)	74	130.2(108.4-188.4)	20.1	1.30 (0.89-1.88)	1.20 (0.81-1.77)
<i>P_{trend}</i>				0.432	0.746				0.311	0.596

M2-polarized macrophages

Q1	72	0.0 (0.0-4.40)	14.3	1.00 (reference)	1.00 (reference)	72	0.0(0.0-4.4)	25.8	1.00 (reference)	1.00 (reference)
Q2	73	12.7 (9.0-16.6)	12.3	1.27 (0.86-1.87)	0.92 (0.61-1.40)	75	12.9 (9.0-16.6)	20.0	1.22 (0.84-1.78)	1.02 (0.69-1.50)
Q3	74	40.6 (30.2-56.3)	11.1	1.32 (0.89-1.96)	1.11 (0.73-1.68)	75	40.7(30.2-56.3)	18.4	1.40 (0.97-2.03)	1.14 (0.77-1.70)
Q4	73	145.6 (95.6-212.8)	11.1	1.41 (0.96-2.06)	1.34 (0.89-2.01)	74	144.4(93.8-212.8)	17.8	1.42 (0.98-2.06)	1.23 (0.83-1.83)
<i>P_{trend}</i>				0.156	0.071				0.119	0.250

^aM1-polarized macrophages were defined as macrophages in the 4th and M2-polarized macrophages as macrophages in the 1st quartile of M1-M2-index distribution.

^bCox proportional hazards regression model adjusted for age, sex, pathologic N stage (N0, N1, Nx), tumor grade (well/moderately differentiated, poorly differentiated, unknown), lymphovascular invasion (negative, positive, unknown), resection margin status (R0, R1, R2, unknown), receipt of adjuvant treatment. Disease-free survival: n=292; overall survival: n=296.

Abbreviations: CI:confidence interval; HR:hazard ratio; IQR:interquartile range; Q:quartile

Supplementary Table S12. Univariable and multivariable Cox regression models for disease-free and overall survival according to Gcross spatial measurements between tumor cells and M1- and M2-polarized macrophages.

Gross function measurements ^a	Disease-free survival					Overall survival				
	No. of patients	Median, IQR (cells/mm ²)	Median survival (months)	Univariable HR (95% CI)	Multivariable HR (95% CI) ^b	No. of patients	Median, IQR (cells/mm ²)	Median survival (months)	Univariable HR (95% CI)	Multivariable HR (95% CI) ^b
10µm radius										
G_{tumor}:M1										
Q1	72	0.003(0.001-0.004)	17.1	1.00 (reference)	1.00 (reference)	73	0.003 (0.002-0.004)	25.8	1.00 (reference)	1.00 (reference)
Q2	73	0.008(0.006-0.009)	12.3	1.33 (0.89-1.97)	1.10 (0.72-1.67)	75	0.007 (0.006-0.009)	16.8	1.40 (0.97-2.02)	1.19 (0.80-1.77)
Q3	74	0.01(0.01-0.02)	11.1	1.23 (0.83-1.83)	1.06 (0.69-1.63)	74	0.01 (0.01-0.02)	19.7	1.25 (0.86-1.80)	0.99 (0.65-1.49)
Q4	73	0.03(0.02-0.04)	10.8	1.20 (0.81-1.77)	1.00 (0.65-1.52)	74	0.03 (0.02-0.04)	20.3	1.14 (0.79-1.65)	0.87 (0.59-1.28)
<i>P_{trend}</i>				0.642	0.800				0.897	0.223
G_{tumor}:M2										
Q1	73	0.001 (0.001-0.001)	14.4	1.00 (reference)	1.00 (reference)	73	0.001 (0.001-0.001)	25.3	1.00 (reference)	1.00 (reference)
Q2	73	0.003 (0.003-0.004)	12.1	1.33 (0.90-1.98)	1.35 (0.90-2.03)	74	0.003 (0.003-0.004)	20.9	1.17 (0.80-1.71)	1.22 (0.83-1.78)
Q3	73	0.008 (0.007-0.010)	11.1	1.51 (1.01-2.26)	1.46 (0.96-2.22)	75	0.008 (0.007-0.010)	20.4	1.42 (0.98-2.07)	1.36 (0.92-1.99)
Q4	73	0.02 (0.02-0.03)	10.0	1.77 (1.20-2.62)	1.80 (1.21-2.68)	74	0.02 (0.02-0.03)	18.2	1.70 (1.18-2.45)	1.50 (1.02-2.19)
<i>P_{trend}</i>				0.006	0.007				0.004	0.064
20µm radius										
G_{tumor}:M1										
Q1	73	0.03(0.02-0.04)	14.3	1.00 (reference)	1.00 (reference)	74	0.03(0.02-0.04)	25.8	1.00 (reference)	1.00 (reference)
Q2	73	0.06(0.05-0.07)	13.8	1.29 (0.87-1.92)	1.22 (0.80-1.84)	75	0.06(0.05-0.07)	20.9	1.38 (0.95-2.01)	1.34 (0.90-1.99)
Q3	73	0.10(0.09-0.11)	11.5	1.17 (0.78-1.74)	1.11 (0.72-1.71)	73	0.1(0.09-0.11)	18.2	1.18 (0.82-1.71)	0.98 (0.65-1.47)
Q4	73	0.18(0.15-0.23)	10.3	1.35 (0.91-1.98)	1.10 (0.72-1.68)	74	0.18(0.15-0.23)	20.1	1.37 (0.94-1.98)	1.04 (0.71-1.54)
<i>P_{trend}</i>				0.222	0.939				0.209	0.730
G_{tumor}:M2										
Q1	73	0.009(0.005-0.014)	15.5	1.00 (reference)	1.00 (reference)	73	0.009 (0.005-0.013)	25.3	1.00 (reference)	1.00 (reference)
Q2	73	0.03(0.02-0.03)	13.1	1.41 (0.94-2.11)	1.23 (0.81-1.88)	74	0.03(0.02-0.03)	20.9	1.37 (0.94-1.99)	1.32 (0.88-1.96)
Q3	73	0.06(0.05-0.07)	11.1	1.52 (1.02-2.26)	1.55 (1.01-2.39)	75	0.06(0.05-0.07)	20.5	1.34 (0.92-1.95)	1.10 (0.73-1.65)
Q4	73	0.13(0.11-0.18)	10.2	1.83 (1.25-2.70)	1.72 (1.14-2.60)	74	0.13(0.11-0.18)	17.7	1.74 (1.21-2.51)	1.59 (1.08-2.35)
<i>P_{trend}</i>				0.004	0.009				0.007	0.114
30 µm radius										
G_{tumor}:M1										
Q1	71	0.07 (0.06-0.10)	14.1	1.00 (reference)	1.00 (reference)	73	0.07 (0.06-0.10)	23.9	1.00 (reference)	1.00 (reference)
Q2	74	0.15 (0.13-0.18)	14.1	1.08 (0.72-1.61)	1.02 (0.67-1.55)	75	0.15 (0.13-0.18)	24.4	1.25 (0.86-1.82)	1.11 (0.74-1.65)
Q3	73	0.25 (0.21-0.27)	13.6	1.00 (0.67-1.48)	0.90 (0.59-1.37)	75	0.24 (0.21-0.27)	18.2	1.09 (0.75-1.58)	0.93 (0.62-1.38)
Q4	74	0.40 (0.33-0.49)	10.3	1.18 (0.80-1.73)	0.91 (0.60-1.39)	73	0.40 (0.33-0.49)	20.3	1.27 (0.88-1.84)	0.96 (0.65-1.42)
<i>P_{trend}</i>				0.440	0.596				0.325	0.637

G_{tumor:M2}										
Q1	73	0.03 (0.02-0.04)	14.9	1.00 (reference)	1.00 (reference)	74	0.03 (0.02-0.04)	25.3	1.00 (reference)	1.00 (reference)
Q2	73	0.07 (0.06-0.09)	11.1	1.50 (1.01-2.24)	1.43 (0.95-2.16)	74	0.07 (0.06-0.09)	21.0	1.45 (1.00-2.10)	1.57 (1.08-2.30)
Q3	72	0.15 (0.12-0.17)	9.9	1.55 (1.04-2.31)	1.64 (1.07-2.51)	74	0.15 (0.12-0.17)	20.1	1.39 (0.95-2.01)	1.25 (0.84-1.87)
Q4	74	0.29 (0.25-0.35)	12.3	1.65 (1.12-2.44)	1.68 (1.12-2.52)	74	0.29 (0.25-0.35)	18.4	1.59 (1.10-2.30)	1.49 (1.01-2.18)
<i>P_{trend}</i>				0.028	0.025				0.038	0.164

^aKaplan-Meier edge corrected G_{cross} function values measured as the probability of finding at least one macrophage/M1-polarized macrophage/M2-polarized macrophage within a 10µm, 20µm or 30µm radius from a tumor cell. M1-polarized macrophages were defined as macrophages in the 4th and M2-polarized macrophages as macrophages in the 1st quartile of M1-M2-index distribution.

^bCox proportional hazards regression model adjusted for age, sex, pathologic N stage (N0, N1, Nx), tumor grade, well/moderately differentiated, poorly differentiated, unknown), lymphovascular invasion (negative, positive, unknown), resection margin status (R0, R1, R2, unknown), and receipt of adjuvant treatment. Disease-free survival: n=292; overall survival: n=296.

Abbreviations: CI:confidence interval; HR:hazard ratio; IQR:interquartile range; Q:quartile

Supplementary Table S13. Disease-free survival according to combined M2-polarized macrophage density and Cross spatial distance function between tumor cells and M2-polarized macrophages.

Combined density and spatial groups ^a	No. of patients	Disease-free survival		
		Median survival (months)	Univariable HR (95% CI)	Multivariable HR (95% CI) ^b
10µm radius				
Dens _{Low} -Spatial _{Low}	113	14.3	1.00 (reference)	1.00 (reference)
Dens _{Low} -Spatial _{High}	31	7.0	1.69 (0.99-2.73)	1.18 (0.71-1.95)
Dens _{High} -Spatial _{Low}	32	14.1	1.10 (0.67-1.80)	1.15 (0.70-1.89)
Dens _{High} -Spatial _{High}	116	11.6	1.38 (1.01-1.87)	1.52 (1.10-2.09)
<i>P_{interaction}</i>			0.196	0.224
20µm radius				
Dens _{Low} -Spatial _{Low}	117	14.1	1.00 (reference)	1.00 (reference)
Dens _{Low} -Spatial _{High}	27	7.0	1.44 (0.90-2.32)	1.15 (0.67-1.98)
Dens _{High} -Spatial _{Low}	28	14.1	0.94 (0.55-1.61)	1.02 (0.59-1.76)
Dens _{High} -Spatial _{High}	120	11.5	1.37 (1.01-1.86)	1.54 (1.12-2.13)
<i>P_{interaction}</i>			0.077	0.035
30µm radius				
Dens _{Low} -Spatial _{Low}	116	13.6	1.00 (reference)	1.00 (reference)
Dens _{Low} -Spatial _{High}	31	10.1	1.17 (0.72-1.89)	0.94 (0.55-1.62)
Dens _{High} -Spatial _{Low}	31	14.1	0.92 (0.55-1.56)	0.97 (0.57-1.64)
Dens _{High} -Spatial _{High}	118	11.1	1.31 (0.97-1.78)	1.50 (1.09-2.07)
<i>P_{interaction}</i>			0.252	0.109

^aCombined M2-polarized macrophage density and spatial groups were defined using the median according to the distribution of M2-polarized macrophage density and $G_{\text{tumor:M2}}$ measurements within 10µm, 20 µm and 30 µm radii. M2-polarized macrophages were defined as macrophages in the 1st quartile of M1-M2-index distribution and Kaplan-Meier edge corrected Gcross function values were measured as the probability of finding at least one M2-polarized macrophage within a 10µm, 20µm or 30µm radius from a tumor cell.

^bCox proportional hazards regression model adjusted for age, sex, pathologic N stage (N0, N1, Nx), tumor grade (well/moderately differentiated, poorly differentiated, unknown), lymphovascular invasion (negative, positive, unknown), resection margin status (R0, R1, R2, unknown), and receipt of adjuvant treatment. Disease-free survival: n=292.

Abbreviations: CI:confidence interval; HR:hazard ratio

Supplementary Table S14. Univariable and multivariable Cox regression models for disease-free survival according to density-adjusted G_{tumor:M2} Gross spatial measurements between tumor cells and M2-polarized macrophages within 20 µm radius.

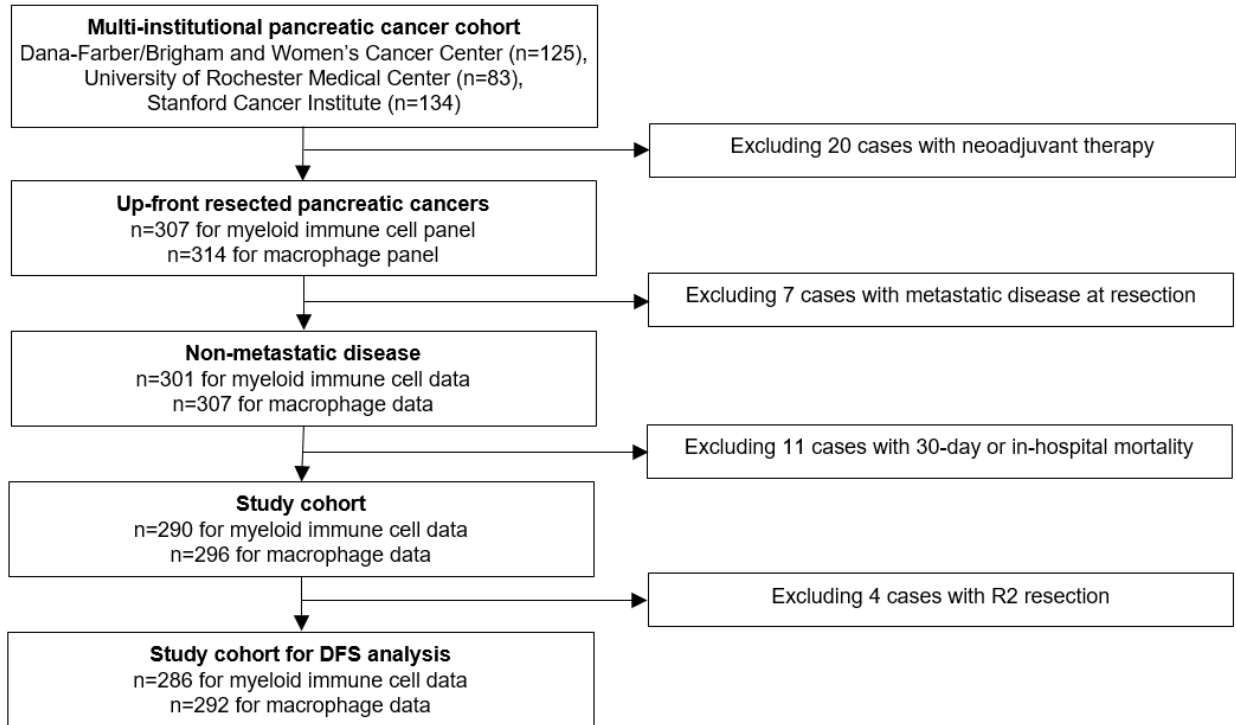
Density-adjusted G _{tumor:M2}	No. of patients	Median, IQR (model residual)	Median survival (months)	Univariable HR (95% CI)	Multivariable1 HR (95% CI) ^b	Multivariable2 HR (95% CI) ^c
Q1	71	-1.0 (-1.6-0.6)	13.4	1.00 (reference)	1.00 (reference)	1.0 (reference)
Q2	75	-0.1 (-0.2-0.0)	14.2	0.99 (0.97-1.01)	1.21 (0.81-1.82)	1.21 (0.80-1.81)
Q3	74	0.3 (0.2-0.4)	11.9	1.08 (0.95-1.23)	1.31 (0.88-1.96)	1.30 (0.87-1.95)
Q4	72	1.0 (0.8-1.2)	9.9	1.23 (0.91-1.68)	1.59 (1.07-2.36)	1.59 (1.07-2.36)
P _{trend}				0.07	0.02	0.02

^aKaplan-Meier edge corrected G_{tumor:M2} function values measured as the probability of finding at least one M2-polarized macrophage within a 20 µm radius from a tumor cell. M2-polarized macrophages were defined as macrophages in the 1st quartile of M1-M2-index distribution.

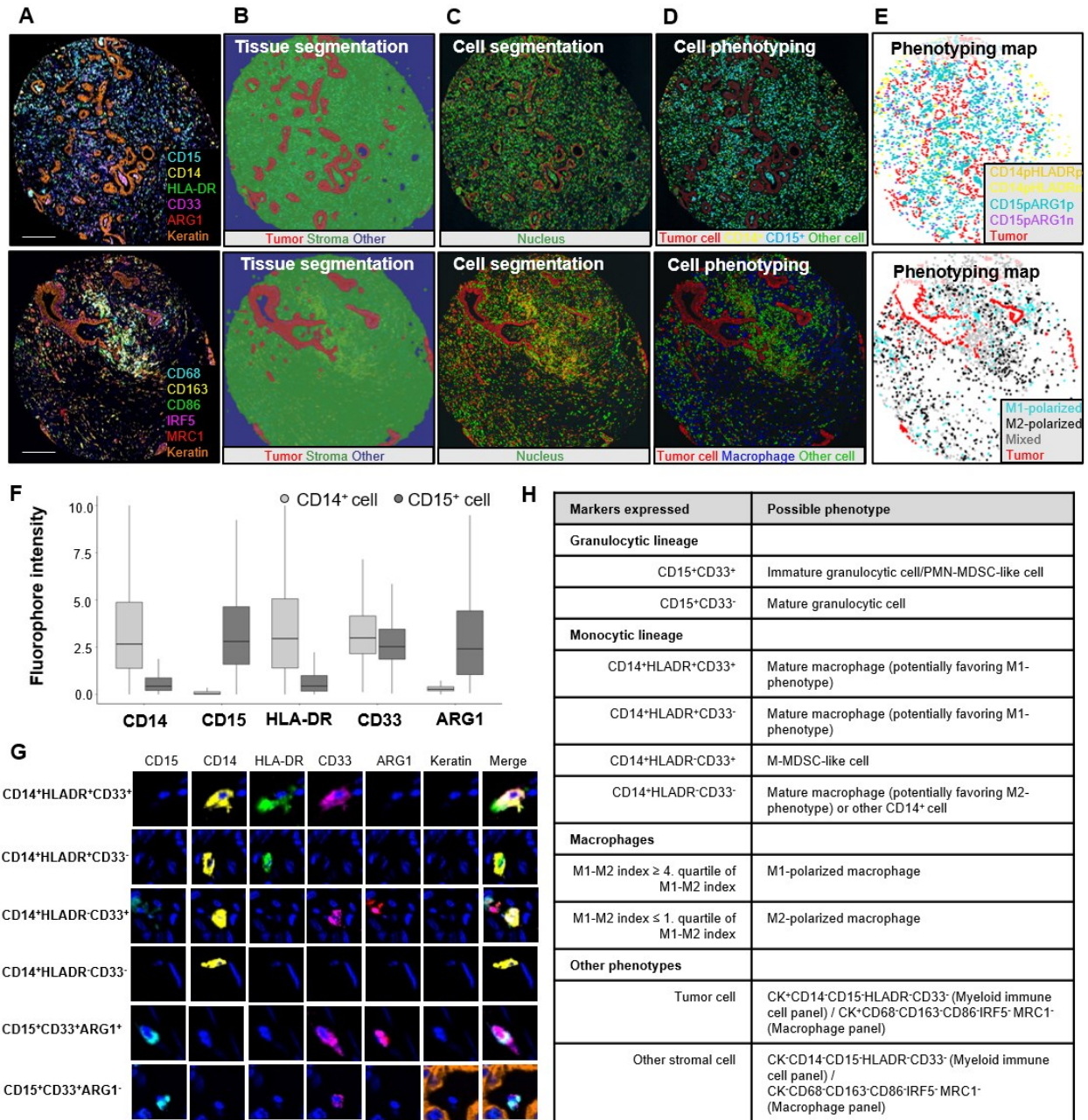
^bCox proportional hazards regression model adjusted for age, sex, pathologic N stage (N0, N1, Nx), tumor grade (well/moderately differentiated, poorly differentiated, unknown), lymphovascular invasion (negative, positive, unknown), resection margin status (R0, R1, R2, unknown), and receipt of adjuvant treatment. Disease-free survival: n=292.

^cAdditionally adjusted for M2-polarized macrophage density.

Abbreviations: CI:confidence interval; HR:hazard ratio; IQR:interquartile range; Q:quartile

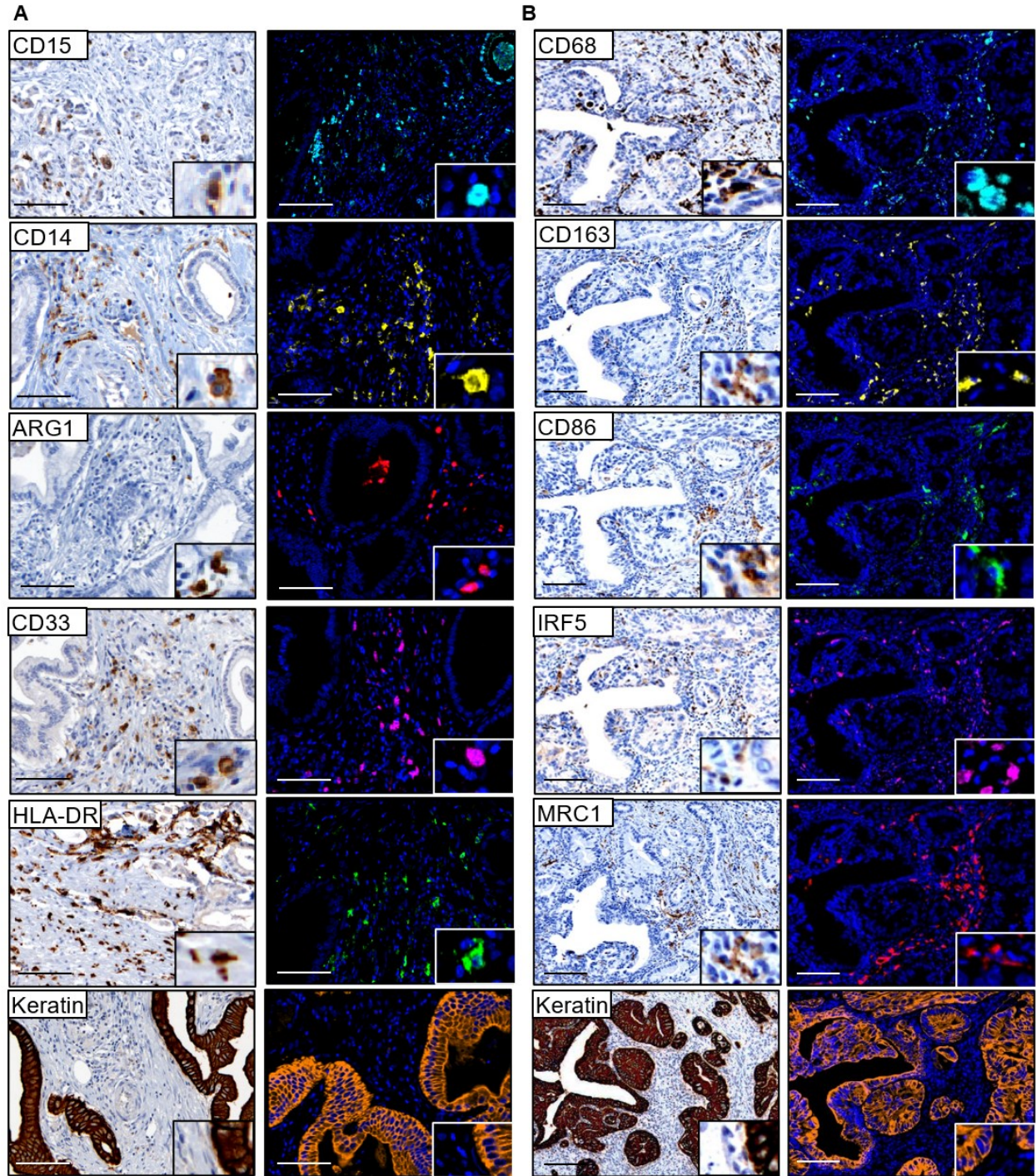


Supplementary Figure S1. Flow chart of the study cohort for outcome analyses.



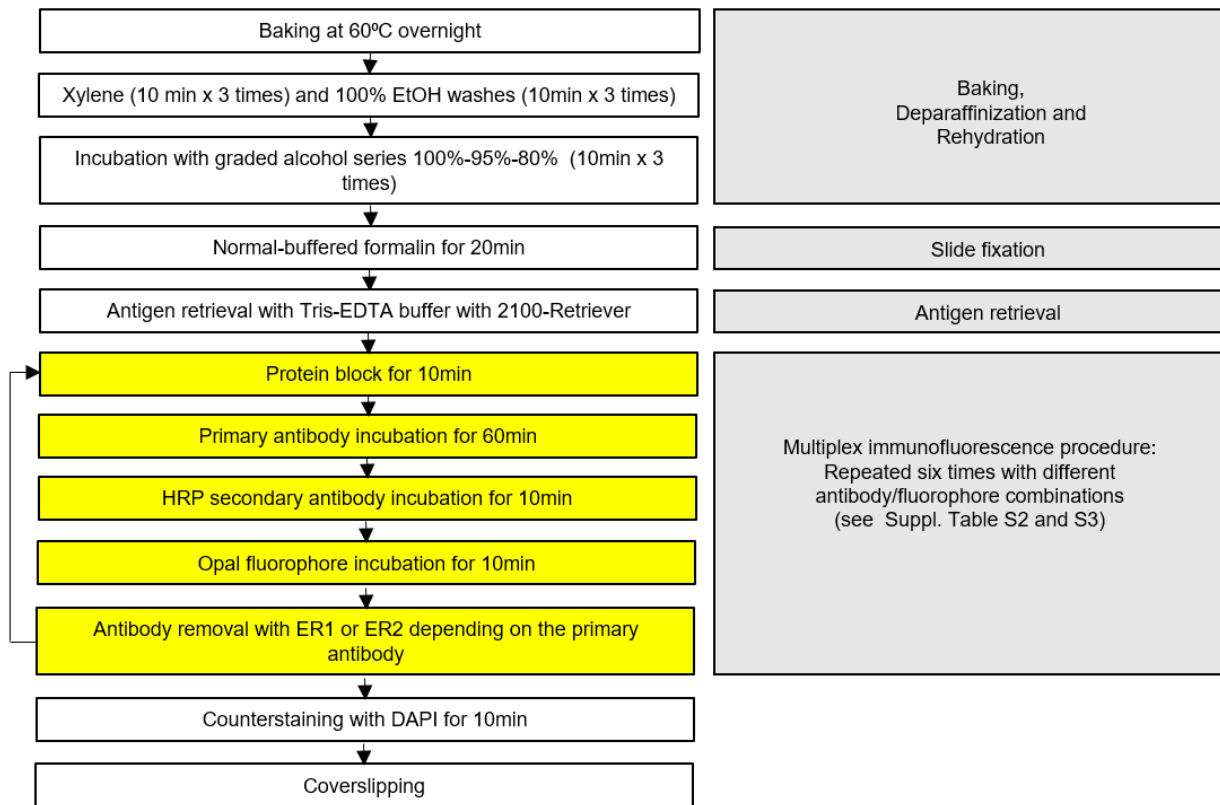
Supplementary Figure S2. Methodology and gating strategy for myeloid immune cell detection.

Example images of myeloid cell and macrophage panels (A). Sequential analysis steps included tissue compartment segmentation (B), cell segmentation (C), and cell phenotyping (D). Phenotyping maps generated with the R Statistical programming language show examples of detected phenotypes with myeloid immune cell and macrophage panels (E). Fluorophore signal intensities in monocytic (CD14⁺) and granulocytic cells (CD15⁺) (F). Details of detected phenotypes from myeloid immune cell and macrophage panels (G and H). The scale bar is 200 μm. Abbreviations: M-MDSC: monocytic myeloid-derived suppressor cell; PMN-MDSC: polymorphonuclear myeloid-derived suppressor cell.



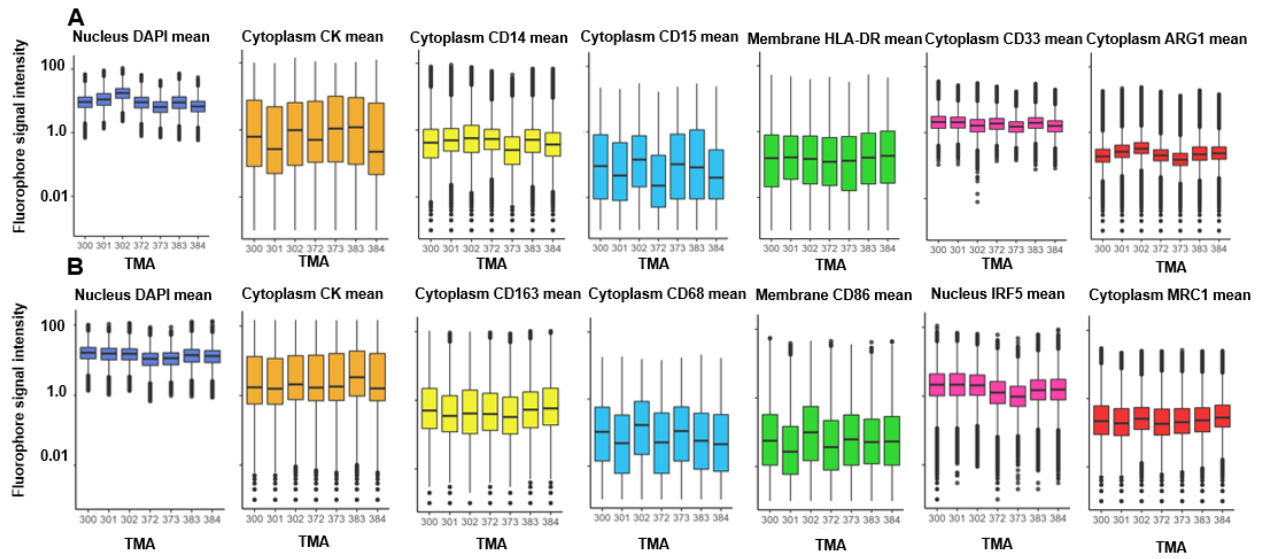
Supplementary Figure S3. Comparison of staining patterns between chromogenic immunohistochemistry (IHC) and multiplex immunofluorescence (mIF).

Myeloid cell (A) and macrophage (B) markers showed comparable staining patterns between monoplex IHC and mIF. The scale bar is 100 μm .

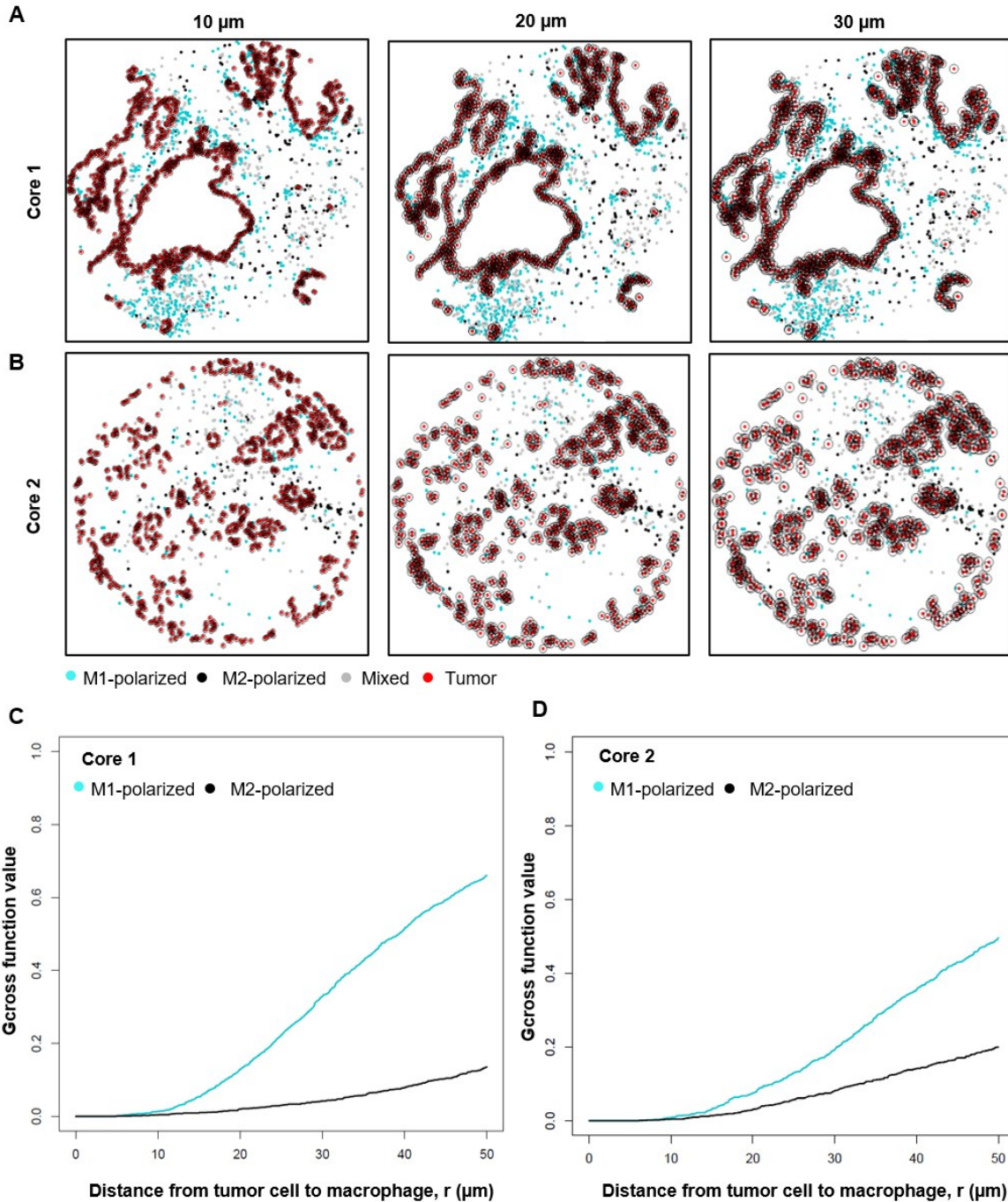


Supplementary Figure S4. Flow chart of the cyclic immunofluorescence procedure.

The repeated steps in cyclic multiplex immunofluorescence procedure (yellow) were performed with a Leica BOND RX Research automated staining instrument.

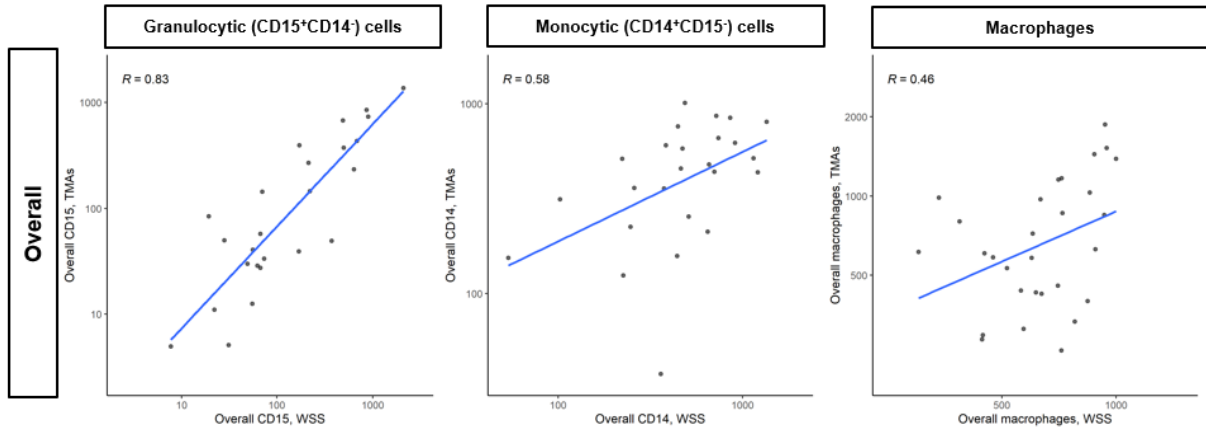


Supplementary Figure S5. Fluorophore signal intensities across resected pancreatic cancer tissue microarrays (TMA) for myeloid immune cell (A) and macrophage (B) panel markers. X axis labels indicate identification numbers of seven study TMAs.



Supplementary Figure S6. Examples of spatial Gcross function analysis between tumor cells and macrophage populations.

$G_{\text{tumor:M1}}(r)$ evaluates the probability of a tumor cell being co-located with at least one M1-polarized macrophage and $G_{\text{tumor:M2}}(r)$ the probability of co-location with at least one M2-polarized macrophage within a specified radius, r (examples 10 μm , 20 μm , and 30 μm) (A-B). The output curves showing the function value with each radius indicate that, in these two example cores, the probability of a tumor cell being co-located with at least one M1-polarized macrophage is higher than the probability of co-location with a M2-polarized macrophage at all tested radii (C-D).

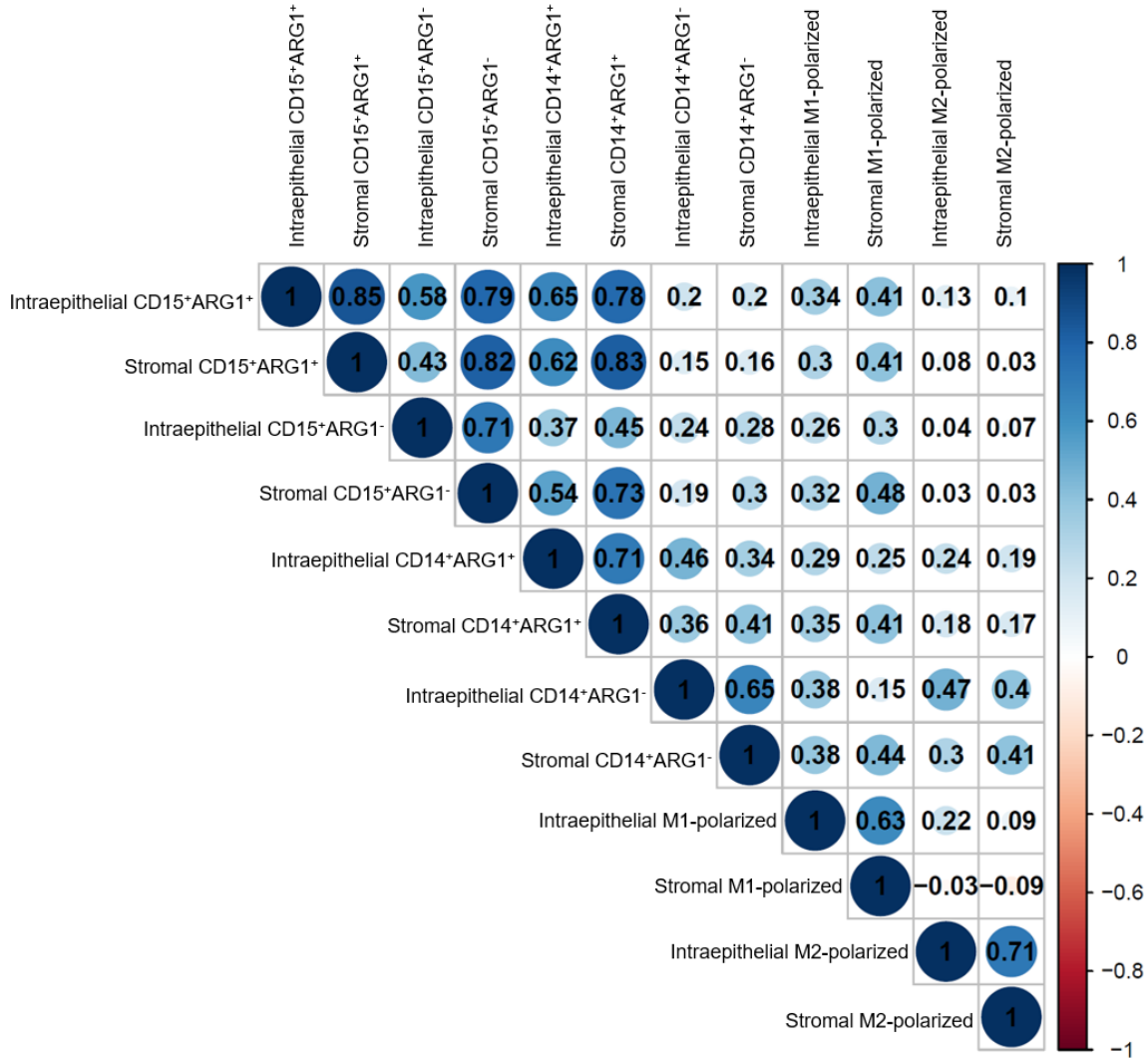


Supplementary Figure S7. Correlations between tissue microarray cores and whole-slide sections of myeloid immune cell densities.

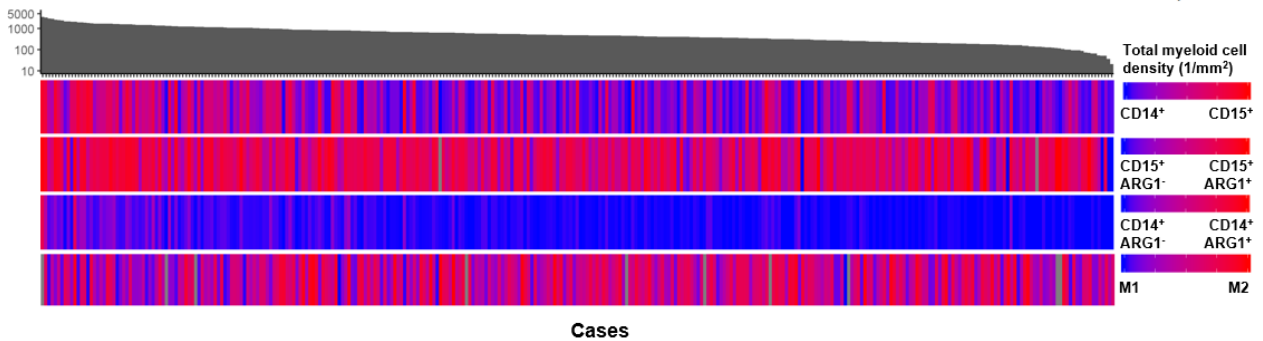
Spearman correlation coefficients (R) were calculated between 29 randomly selected cases with macrophage data and 27 randomly selected cases with MDSC data. On average, 5.5 images (1.36 mm² per image) were obtained from whole-slide sections and the Spearman correlation coefficients for granulocytic cell (CD15⁺CD14⁻), monocytic cell (CD14⁺CD15⁻) and macrophage densities were calculated between the tissue microarray cores and the whole-slide sections.

Abbreviations: WSS: whole-slide section; TMA: tissue-microarray

A

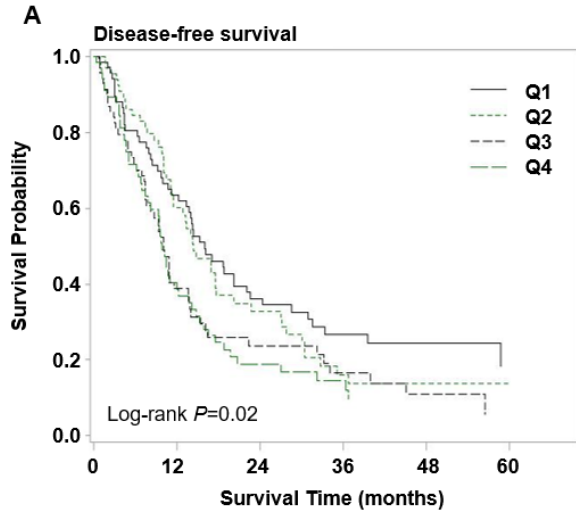


B

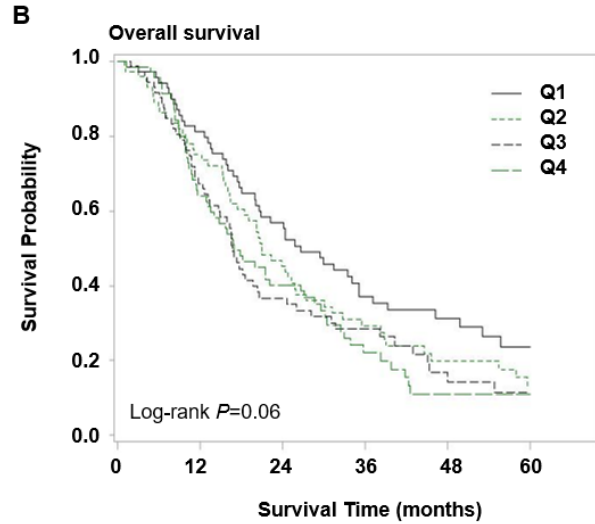


Supplementary Figure S8. Distribution of myeloid immune cell densities.

Spearman correlation coefficients of myeloid immune cell densities in tumor intraepithelial and stromal compartments (A). Myeloid cell distributions across the study cohort (n=290) according to decreasing total myeloid cell density (top grey bar plot) (C). The heatmaps display the relative distributions (0-100%) of the specified myeloid cell populations within the parent populations (first row: all CD14⁺ or CD15⁺ myeloid cells; second row: CD15⁺ myeloid cells; third row: CD14⁺ myeloid cells; fourth row M1- or M2-polarized macrophages); grey bars indicate missing data. (B).



		Number at Risk (Time, months)					
Quartile	0	12	24	36	48	60	
Q1	72	41	21	12	10	3	
Q2	71	33	16	7	5	4	
Q3	73	23	10	7	4	1	
Q4	70	22	10	6	4	4	



		Number at Risk (Time, months)					
Quartile	0	12	24	36	48	60	
Q1	72	55	36	20	14	6	
Q2	73	53	29	16	10	5	
Q3	73	46	22	15	6	4	
Q4	72	44	25	11	5	5	

Supplementary Figure S9. Kaplan-Meier survival curves for CD15⁺ARG1⁺ cell density.

Kaplan-Meier survival curves for CD15⁺ARG1⁺ cell density for disease-free survival (A) and overall survival (B). P values were calculated with log-rank test.