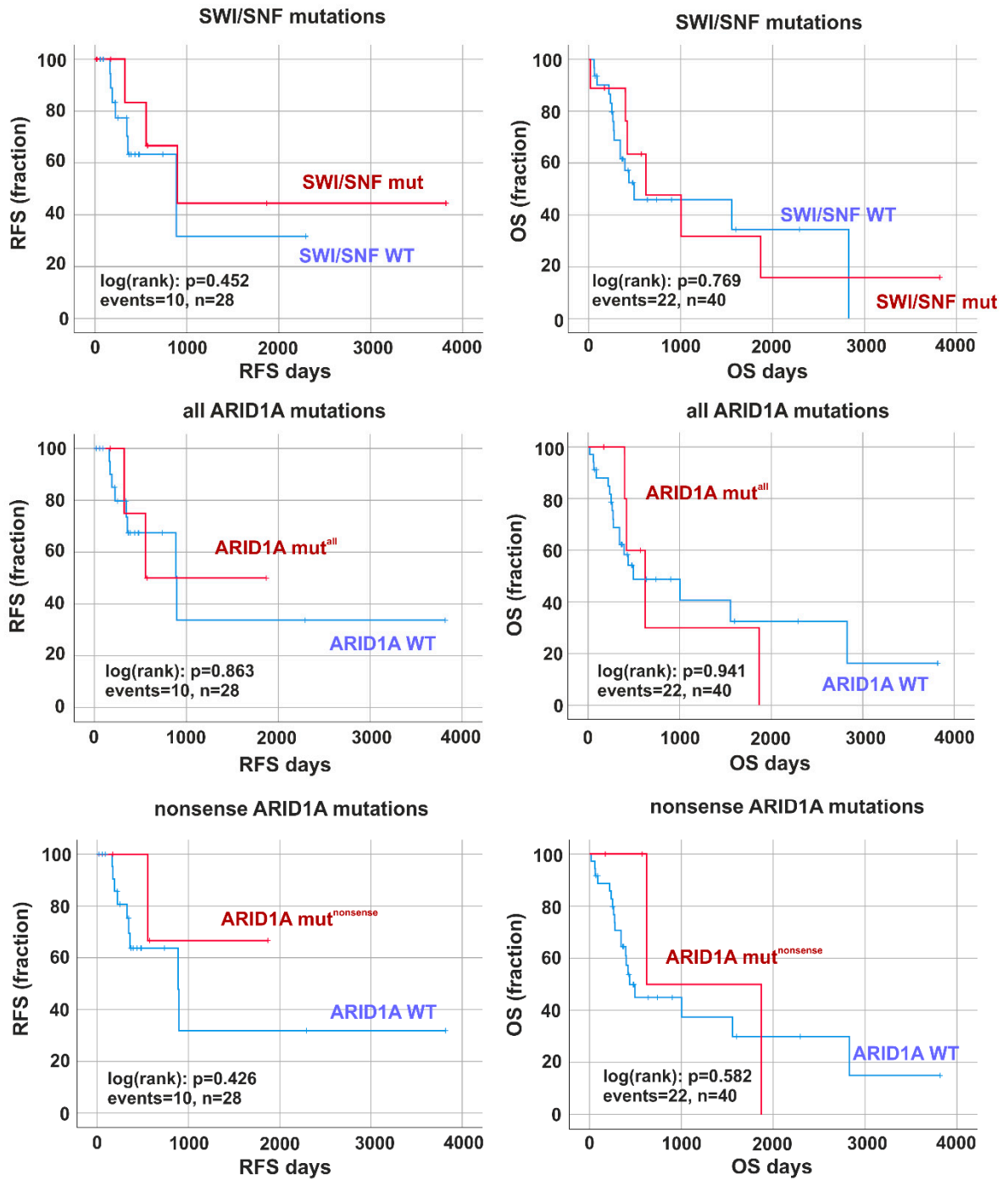
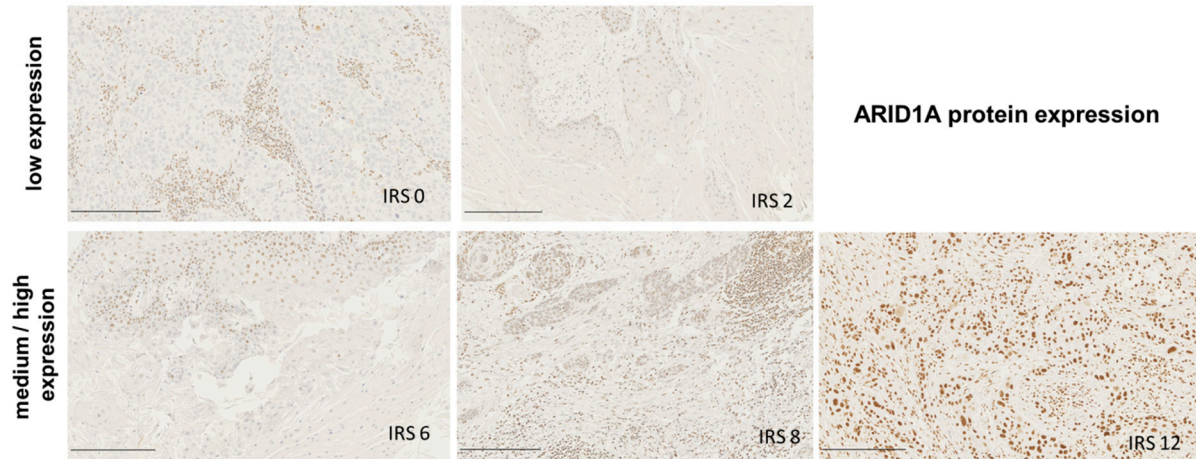


**Supplemental Figure 1: Study design of the project.** *Left box:* Discovery study. TCGA data sets of carcinomas with histologically squamous differentiation ( $n=3$  pure SCC and  $n=43$  MIX) were analyzed for genetic alterations of seven frequently affected subunits of the SWI/SNF complexes BAF and PBAF. In a second step *ARID1A* mutations were correlated with ARID1A protein expression. *Right box:* Validation study. Protein expression of seven SWI/SNF complex proteins (*ARID1A*, *SMARCA4*, *SMARCB1*, *SMARCC1*, *SMARCC2*, *SMARCA2* and *PBRM1*) was assessed by immunohistochemistry in our own sq-BLCA sample cohort. In a second step tumor samples with *ARID1A* expression loss (IRS0-2) underwent NGS panel sequencing for putative genetic alterations of the *ARID1A* gene. Finally, we analyzed whether a co-occurrence of *ARID1A* expression loss, genetic alterations and genetic driver mutations (*TP53* and *FGFR3* (\*Rose, M. et al. 2020 [5]); *PIK3CA* and *CDKN2A* (\*\*unpublished so far)) and PD-L1 expression (\*\*\*)Morsch, R. et al. 2020 [44]) could be found. In parallel, *ARID1A* expression loss and genetic alterations were used for both univariate Kaplan-Meier and correlation analysis with clinico-pathological characteristics, however, with no statistical significance.



**Supplemental Figure 2: Prognostic impact of SWI/SNF and ARID1A mutations on tumor patients' survival.** Univariate survival analysis illustrates that tumors with at least a single mutation in one/or more analyzed SWI/SNF components (top row, red curve) or ARID1A mutations (all (middle row) or nonsense (bottom row), red curves) predict no significant shorter RFS / OS compared to the WT status (blue curves, respectively).



**Supplemental Figure 3: Immunohistochemical staining of ARID1A according to calculated IRS.**  
ARID1A staining is shown for IRS 0, 2, 6, 8 and 12 (Black scale bar: 250  $\mu$ M).

**Supplementary Table 1: Primer sequences for Sanger sequencing of FFPE Material.**

Gene	Primer sequence	Annealing Temperature
TP53		
Exon 5	5'-TGCCGT CTTCCAGTTGCTTTATC-3'	60°C
	5'-GCAATCAGTGAGGAATCAGAGGC-3'	
Exon 6	5'-AGCAGCTGGGGCTGGAGAG-3'	63°C
	5'-CTGGAGGCCCACTGACAAC-3'	
Exon 7	5'-CCAAGGCGCACTGGCCTCA-3'	63°C
	5'-AGAGGCAAGCAGAGGCTGG-3'	
Exon 8	5'-CTGATTTCTTACTGCCTC-3'	60°C
	5'-CTGCACCCTTGGTCTCCTC-3'	
Exon 9	5'-GTTATGCCTCAGATTCATT-3'	55°C
	5'-CGGCATTTTGAGTGTTAGAC-3'	
CDKN2A		
Exon 1	5'-GCTTCCTTTCCGTCATGC-3'	59°C
	5'-CAGGTACCGTGCGACATC-3'	
Exon 2	5'-CTGTTCTCTCTGGCAGGTCA-3'	59°C
	5'-TGTGCTGGAAAATGAATCCT-3'	
Exon 2	5'-CTTCCTGGACACGCTGGT-3'	59°C
	5'-TGGAGGCTCTCAGGGTACAAA-3'	

Supplementary Table 2: Clinico-pathological parameters of the TCGA sq-BLCA data set in relation to SWI/SNF mutations.

	<i>n</i> <sup>a</sup>	SWI/SNF mutations <sup>b</sup>		P-value <sup>c</sup>
		negative	positive	
<b>Parameter:</b>				
Tumor stage				
pT2	13	10	3	0.876
pT3-pT4	24	19	5	
Lymph node status				
neg	26	19	7	0.281
pos	10	9	1	

<sup>a</sup>Only patients of the TCGA platform with squamous histology were included;

<sup>b</sup>criteria: SWI/SNF mutation is defined if at least one genetic alteration (missense/nonsense) in one/or more of the analyzed components is present;

<sup>c</sup>Fisher's exact test

Supplementary Table 3: Clinico-pathological parameters of the TCGA sq-BLCA data set in relation to all identified *ARID1A* mutations.

	<i>n</i> <sup>a</sup>	ARID1A mutations <sup>b</sup>		P-value <sup>c</sup>
		negative	positive	
<b>Parameter:</b>				
Tumor stage				
pT2	13	11	2	0.809
pT3-pT4	24	21	3	
Lymph node status				
neg	26	22	4	0.680
pos	10	9	1	

<sup>a</sup>Only patients of the TCGA platform with squamous histology were included;

<sup>b</sup>criteria: genetic alterations of *ARID1A* independent of mutation type; <sup>c</sup>Fisher's exact test

Supplementary Table 4: Clinico-pathological parameters of the TCGA sq-BLCA data set in relation to nonsense *ARID1A* mutations.

	<i>n</i> <sup>a</sup>	ARID1A mutations <sup>b</sup>		P-value <sup>c</sup>
		negative	positive	
<b>Parameter:</b>				
Tumor stage				
pT2	13	11	2	0.239
pT3-pT4	24	23	1	
Lymph node status				
neg	26	24	2	0.825
pos	10	9	1	

<sup>a</sup>Only patients of the TCGA platform with squamous histology were included;

<sup>b</sup>criteria: Only nonsense *ARID1A* mutation were included; <sup>c</sup>Fisher's exact test

Supplementary Table 5: Overlap of ARID1A mutations / expression loss with PD-L1 expression.

	ARID1A mut/del	ARID1A exp (IRS≤2)
<b>PD-L1 scores for antibody clone 28-8</b>	<b>n</b>	<b>n</b>
<b>IC ≥ 5%<sup>a</sup></b>	1/3	2/6
<b>CPS ≥ 10<sup>b</sup></b>	0/3	1/6

<sup>a</sup>atezolizumab , <sup>b</sup>pembrolizumab first line therapy requirement

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**Supplementary Table 6: Abbreviation list**

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AKT	serine/threonine protein kinase B
ARID1A	AT-rich interactive domain-containing protein 1A
BAF	BRG1/BRM associated factor
BRG1	alias symbol for SMARCA4
BRM	alias symbol for SMARCA2
cBAF	canonical BRG1/BRM associated factor
CDKN2A	cyclin dependent kinase inhibitor 2A
CNV	copy number variation
COSMIC	Catalogue Of Somatic Mutations In Cancer
CPS	Combined Positivity Score
CXCL13	C-X-C motif chemokine ligand 13
dbSNP	Single Nucleotide Polymorphism Database
DNA	Deoxyribonucleic acid
DSB	double strand break
EMA	European Medicines Agency
F.A.	Fabian Achenbach
FFPE	formalin-fixed paraffin-embedded
FGFR3	fibroblast growth factor receptor 3
HDAC6	histone deacetylase 6
H&E	hematoxylin and eosin stain
HGNC	HUGO Gene Nomenclature Committee (HUGO: Human Genome Organisation)
ICI	immune checkpoint inhibitor
IC(-score)	immune cell score
ID	identification
IRS	Immune Reactive Score
MUT	mutated
ncBAF	non-canonical BRG1/BRM associated factor
NGS	next generation sequencing
NOS	not otherwise specified
N.T.G.	Nadine Therese Gaisa
PBAF	polybromo-associated BRG1/BRM associated factor
PBRM1	Protein polybromo-1
PCR	polymerase chain reaction
PD-L1	Programmed death-ligand 1
PIK3CA	phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha
RWTH	Rheinisch-Westfälische Technische Hochschule
SCC	squamous cell carcinoma
SMARCA2	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 2
SMARCA4	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 4
SMARCB1	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily b, member 1
SMARCC1	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily c, member 1
SMARCC2	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily c, member 2
SPSS	Statistical Package for the Social Sciences
sq-BLCA	squamous (differentiated) bladder cancer
SWI/SNF	SWItch/Sucrose Non-Fermentable
TCGA	The Cancer Genome Atlas
TMA	Tissue microarrays
TP53	tumor protein p53
UTR	untranslated region
WHO	World Health Organization
WT	wildtype

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