

Treatment approach						
„Conservative“	„Progressive“	CIViC	ESMO	NCT	JCR	EDRN
		A: Proven/consensus association in human medicine B: Clinical trial or other primary patient data supports association	I A: Prospective randomized trial I B: Prospective non-randomized trial I C: Basket trials and trials across disease types II A: Retrospective studies II B: Prospective trials; endpoints not currently available	m1 A: Same entity: Prospective study m1 B: Same entity: Retrospective study m1 C: Same entity: Case reports m2 A: Different entity: Prospective study	Tier 1 A: FDA approved therapy/ professional guidelines Tier 1 B: Well-powered studies with expert consensus	Phase 5: Disease burden reduction studies Phase 4: Prospective diagnostic accuracy studies Phase 3: Retrospective studies
		D: In vivo or in vitro models support association E: Indirect evidence	III B: Alteration with predicted impact in same pathway as I IV A: in vivo or in vitro evidence IV B: in silico evidence V: Objective response but not improved outcome	m2 B: Different entity: Retrospective study m2 C: Different entity: Case reports m3: in vitro / in vivo results m4: Biological rationale: no clinical/preclinical data available	Tier 2 C: FDA approval in different entity/ inclusion in clinical trial / multiple small studies with some consensus Tier 2 D: Preclinical trials / case reports	Phase 2: Clinical assay development Phase 1: preclinical exploratory studies
			X: Benign variants		Tier 3: No convincing evidence of cancer association Tier 4: No existing evidence of cancer association	