

Table 1: Summary of effects on survival

	Overall Survival (OS)							Progression free survival (PFS)*	
	Overall HR (95% CI)	Subgroups						Overall HR (95% CI)	Low volume HR (95% CI)
		Low volume HR (95% CI)	High volume HR (95% CI)	De novo HR (95% CI)	Prior local Therapy HR (95% CI)	ECOG 0 HR (95% CI)	ECOG ≥1 HR (95% CI)		
Docetaxel + ADT vs. ADT	0.77 (0.69 - 0.85)	0.91 (0.73 - 1.13)	0.72 (0.63 - 0.84)	0.79 (0.70 - 0.89)	0.90 (0.62 - 1.32)	0.82 (0.71 - 0.93)	0.70 (0.56 - 0.87)	0.67 (0.60 - 0.74)	-
Abiraterone + ADT vs. ADT	0.66 (0.58 - 0.74)	0.67 (0.50 - 0.91)	0.62 (0.53 - 0.71)	0.64 (0.56 - 0.73)	0.94 (0.35 - 2.52)	0.67 (0.56 - 0.80)	0.57 (0.46 - 0.71)	0.46 (0.41 - 0.52)	-
Enzalutamide + ADT vs. ADT	0.63 (0.48 - 0.83)	0.38 (0.21 - 0.69)	0.65 (0.42 - 1.00)	excl.	excl.	excl.	excl.	0.36 (0.30 - 0.44)	-
Apalutamide + ADT vs. ADT	0.65 (0.53 - 0.79)	0.52 (0.35 - 0.78)	0.70 (0.56 - 0.88)	0.68 (0.55 - 0.85)	0.39 (0.22 - 0.69)	0.68 (0.52 - 0.89)	0.56 (0.42 - 0.75)	0.49 (0.39 - 0.62)	-
Abiraterone + ADT vs. Docetaxel + ADT	0.86 (0.73 - 1.01)	-	-	-	-	-	-	0.69 (0.59 - 0.8)	-
Enzalutamide + ADT vs. Docetaxel + ADT	0.82 (0.61 - 1.10)	-	-	-	-	-	-	0.58 (0.44 - 0.77)	-
Apalutamide + ADT vs. Docetaxel + ADT	0.8 (0.68 - 1.06)	-	-	-	-	-	-	0.73 (0.57 - 0.95)	-
Enzalutamide + ADT vs. Abiraterone + ADT	0.96 (0.71 - 1.30)	-	-	-	-	-	-	NS	-
Apalutamide + ADT vs. Abiraterone + ADT	0.99 (0.78 - 1.26)	-	-	-	-	-	-	NS	-
Apalutamide + ADT vs. Enzalutamide + ADT	1.03 (0.74 - 1.45)	-	-	-	-	-	-	NS	-
Radiation + ADT vs. ADT	0.91 (0.81 - 1.03)	0.68 (0.54 - 0.86)	1.07 (0.92 - 1.24)	0.91 (0.92 - 1.03)	-	0.91 (0.79 - 1.05)	0.97 (0.77 - 1.22)	0.96 (0.85 - 1.08) 0.76** (0.69 - 0.84)	0.78 (0.63 - 0.97)

*PFS includes clinical, radiographic and biochemical; ** result for biochemical PFS only; excl. – excluded; NS - non-significant; **Bold** = p value significant

Table 2. Results and GRADE assessment for the direct and indirect evidence from the included studies on the effects of systemic mHSPC treatments and radiotherapy on overall survival

Comparison	Direct Estimate* HR (95%CI)	Direct Estimate* Rating	Indirect Estimate** HR (95%CI)	Indirect Estimate** Rating	NMA Estimate HR (95%CI)	NMA Estimate Rating
Docetaxel + ADT vs. ADT	0.79 (0.71 to 0.89)	High	0.56 (0.38 to 0.81)	Low	0.77 (0.69 to 0.85)	High
Abiraterone + ADT vs. ADT	0.64 (0.56 to 0.73)	Moderate	0.89 (0.60 to 1.34)	Very low ^d	0.66 (0.58 to 0.74)	Moderate ^e
Enzalutamide + ADT vs. ADT	0.63 (0.48 to 0.83)	Low ^{b, c}	-	-	0.63 (0.48 to 0.83)	Low
Apalutamide + ADT vs. ADT	0.65 (0.53 to 0.79)	High	-	-	0.65 (0.53 to 0.79)	High
Abiraterone + ADT vs. Docetaxel + ADT	1.13 (0.77 to 1.66)	Low ^{a, d}	0.81 (0.68 to 0.96)	High	0.86 (0.73 to 1.01)	Moderate ^e
Enzalutamide + ADT vs. Docetaxel + ADT	-	-	0.82 (0.61 to 1.10)	Very low ^d	0.82 (0.61 to 1.10)	Very low ^d
Apalutamide + ADT vs. Docetaxel + ADT	-	-	0.85 (0.68 to 1.06)	Moderate ^d	0.85 (0.68 to 1.06)	Moderate ^d
Enzalutamide + ADT vs. Abiraterone + ADT	-	-	0.96 (0.71 to 1.30)	Very low ^d	0.96 (0.71 to 1.30)	Very low ^d
Apalutamide + ADT vs. Abiraterone + ADT	-	-	0.99 (0.78 to 1.26)	Moderate ^d	0.99 (0.78 to 1.26)	Moderate ^d
Apalutamide + ADT vs. Enzalutamide + ADT	-	-	1.03 (0.74 to 1.45)	Very low ^d	1.03 (0.74 to 1.45)	Very low ^d
Radiotherapy + ADT vs. ADT	0.91 (0.81 to 1.03)	Moderate ^d	-	-	-	-

*direct estimate – effects compared within same study; **indirect estimate – comparisons of effects not compared within the same study. Downgrading due to: ^a = Limitations in study design or execution, ^b = Inconsistency, ^c = Indirectness, ^d = Imprecision, ^e = Incoherence. Legend: ADT = androgen deprivation therapy, HR = hazard ratio, CI = confidence interval, NMA = network meta-analysis. (Adapted from Tables 2 and 4 in the Assessment Report)

Table 3. Summary of cost effectiveness data

	Health Economic Literature review								Cost effectiveness analysis			
	Mean absolute QALYs		Differences in QALYs gained vs. comparator				ICER (USD)		Costs (CHF)	QALYs discounted	Pairwise ICER (CHF) relative to previous non-dominated strategy	Pairwise ICER vs. ADT (CHF)
Time Horizon	3 year	Lifetime	3 year	15 year	20 year	Lifetime	3 year	Lifetime	15 years			
Docetaxel	1.53	5.03	-	-	-	-	-	-	-	-	-	-
Abiraterone	1.73	4.37	-	-	-	-	-	-	-	-	-	-
ADT	1.21	4.02	-	-	-	-	-	-	55,926	3.24	-	-
Docetaxel + ADT vs. ADT	-	-	-	1.06	0.2	-	50,489	4,033	70,956	4.07	18,124	18,124
Abiraterone + ADT vs. ADT (current price of CHF 3529.05)	-	-	-	-	-	-	415,063	188,085	309,089	4.88	-	154,477
<i>Abiraterone + ADT vs. ADT (hypothetical price of CHF 1250.00)*</i>									147,785	4.88		56,012
Abiraterone + ADT vs. Docetaxel + ADT (current price of CHF 3529.05)	-	-	0.2	-	-	1.54	1,009,975	295,212	309,089	4.88	294,163	-
<i>Abiraterone + ADT vs. Docetaxel + ADT (hypothetical price of CHF 1250.00)*</i>									147,785	4.88	97,442	
Enzalutamide + ADT vs. ADT	-	-	-	-	-	-	-	-	361,179	4.93	-	180,872
Enzalutamide + ADT vs. Abiraterone + ADT	-	-	-	-	-	-	-	-	-	-	1,066,633	-
Apalutamide + ADT	-	-	-	-	-	-	-	-	295,750	4.59	dominated	dominated

*the price for Abiraterone is coming under increased pressure with release of generics making price reductions in the near future a possibility