Appendix 3: Summary of findings for the main outcomes.

TKI versus Non-TKI for pediatric Ph+ALL in randomized controlled trial

Patient or population: patients with pediatric Ph+ALL

Intervention: TKI with chemotherapy

Comparison: chemotherapy

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk chemotherapy	Corresponding risk TKI with chemotherapy				
overall survival	**727 per 1000**	**587 per 1000**	**HR 0.68**	90	⊕⊕⊖⊖	
Follow-up: mean 3.1 years		(287 to 901)	(0.26 to 1.78)	(1 study)	**low**[1,2,3]	
event free survival	**614 per 1000**	**451 per 1000**	**HR 0.63**	90	⊕⊕⊖⊖	
Follow-up: mean 3.1 years		(234 to 741)	(0.28 to 1.42)	(1 study)	**low**[1,2,3]	
adverse drug reaction	**774 per 1000**	**635 per 1000**	**RR 0.82**	89	⊕⊕⊖⊖	
Follow-up: mean 3.1 years		(488 to 836)	(0.63 to 1.08)	(1 study)	**low**[1,2,4]	

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio; **HR:** Hazard ratio;

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

[1] blindness was high risk

[2] not applicable

[3] the 95% CI included appreciable benefit or harm

[4] the 95%CI for effect estimates were wide

TKI versus Non-TKI for pediatric Ph+ALL in cohort studies

Patient or population: patients with pediatric Ph+ALL

Intervention: TKIs

Comparison: Non-TKIs

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk Non-TKIs	Corresponding risk TKIs				
overall survival	**340 per 1000**	**99 per 1000** (56 to 177)	**HR 0.25** (0.14 to 0.47)	204 (3 studies)	⊕⊕⊕⊖ **moderate**[1]	
event free survival	**95 per 1000**	**25 per 1000** (12 to 55)	**HR 0.25** (0.12 to 0.56)	110 (2 studies)	⊕⊕⊕⊖ **moderate**[1]	
adverse drug reaction	**561 per 1000**	**566 per 1000** (359 to 891)	**RR 1.01** (0.64 to 1.59)	147 (2 studies)	⊕⊕⊕⊖ **moderate**[1]	

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio; **HR:** Hazard ratio;

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

[1] the magnitude of the treatment effect is large

imatinib versus dasatinib for pediatric Ph+ALL in randomized controlled trial

Patient or population: patients with Ph+ALL

Intervention: imatinib

Comparison: dasatinib

Outcomes	**Illustrative comparative risks* (95% CI)**		**Relative effect (95% CI)**	**No of Participants (studies)**	**Quality of the evidence (GRADE)**	**Comments**
	Assumed risk **Dasatinib**	Corresponding risk **Imatinib**				
overall survival Follow-up: mean 26.4 months	**880 per 1000**	**992 per 1000** (885 to 1000)	**HR 2.26** (1.02 to 5.01)	189 (1 study)	⊕⊕⊖⊖ **low**[1,2,3]	
event free survival Follow-up: mean 26.4 months	**707 per 1000**	**945 per 1000** (789 to 995)	**HR 2.36** (1.27 to 4.39)	189 (1 study)	⊕⊕⊖⊖ **low**[1,2,3]	
adverse drug reaction Follow-up: mean 26.4 months	**596 per 1000**	**578 per 1000** (459 to 733)	**RR 0.97** (0.77 to 1.23)	189 (1 study)	⊕⊕⊖⊖ **low**[1,2,4]	

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio; **HR:** Hazard ratio;

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

[1] the blindness was high risk

[2] not applicable

[3] the 95% CI includes appreciable benefit or harm

[4] the 95%CI for effect estimates were wide