Liver and Lung Toxicity with Bicalutamide in Clinical Trials

Clinical trials involving bicalutamide†:

(("bicalutamide"[All Fields] OR "bicalutamide"[Supplementary Concept]) OR ("ICI-176,334"[All Fields]) OR ("casodex"[All Fields]) OR ("cosudex"[All Fields]) OR ("calutide"[All Fields]) OR ("calumid"[All Fields]) OR ("kalumid"[All Fields])) AND ((clinicaltrial[Filter] OR randomizedcontrolledtrial[Filter]))

(229 results as of 14/09/2021)

RCT = randomised controlled trial, NES = non-experimental study, LFTs = liver function tests; BCLT = bicalutamide; RT = radiotherapy; OCP = oral contraceptive pills

*=Sample size does not include participants in arms that did not receive BCLT.
†=Estimates for severe liver and lung toxicity derived from overall reported incidences within studies (almost invariably 0%) with uncertainty modelled using poisson distributions (95% CIs). Calculated from data in idealistic circumstances (ie: regular liver monitoring and largely excluding participants with abnormal LFTs at baseline).

Severe liver toxicity incidence: 2 events out of 7703 evaluable participants = 0.026% (95% CI: 0.003% to 0.094%) (~1 in 3846)
Severe lung toxicity incidence: 2 events out of 7703 evaluable participants = 0.026% (95% CI: 0.003% to 0.094%) (~1 in 3846)

Combined toxicity incidence: 4 events out of 7703 evaluable participants = 0.052% (95% CI: 0.014% to 0.133%) (~1 in 1923)

Study name or institution of first author	Design	Evaluable participants*	Intervention	Controls	Elevated LFTs	Dropout due to LFTs	Dyspnea	Further notes	Citation(s)
Pitié-Salpêtrière University Hospital	RCT, parallel, open-label	Men with prostate cancer (n = 118)	BCLT 150 mg/day	Orchiectomy or GnRH agonist	NR	0 (0.0%)	0 (0.0%)	Initial dose was 100 mg/day for 19 patients	Châtelain et al., 1994
International Casodex Investigators	RCTs, parallel, open-label and double-blind	Men with prostate cancer and BPH (n = 1452)	BCLT 50 and 150 mg/day	Orchiectomy or Placebo	NR	? (0.3%)	NR	Combined analysis of 8 different studies (some reported prior)	Tyrell, 1994; Iversen et al., 1998
Osaka Medical Center	NES	Men with prostate cancer (n = 16)	BCLT 10–100 mg/day	n/a	3 (18.8%)	0 (0.0%)	NR		Kotake et al., 1996
CCSG	RCT, factorial, double-blind	Men with prostate cancer (n = 404)	BCLT 50 mg/day + GnRH agonist	Flutamide + GnRH agonist	27 (6.7%)	6 (1.5%)	8 (2.0%)	10.5%, 2.4%, 1.5% for LFTs and dyspnea in flutamide arms	Schellhammer et al., 1997; Sarosdy et al.,1998?
IPCPS	RCT, parallel, open-label	Men with prostate cancer (n = 108)	BCLT 150 mg/day	Flutamide + GnRH agonist	1 (0.9%)	1 (0.9%)	NR	1.8% with elevated LFTs in flutamide arm	Boccardo et al., 1999
Abarelix Study Group	RCT, parallel, open-label	Men with prostate cancer (n = 85)	BCLT 150 mg/day + GnRH agonist	GnRH antagonist	2 (2.4%)	2 (2.4%)	NR		Trachtenberg et al., 2002
Early Prostate Cancer Trials (Trial 23, Trial 24, and Trial 25/SPCG-6)	RCTs, parallel, double-blind	Men with prostate cancer (n = *1647*; n = *1798*; 25: n = *607*; All: n = 4022)	BCLT 150 mg/day + Standard care	Placebo + Standard care	23: NR 24: 2.1% 25: 3.1% All: 3.4%	23: NR 24: 0.8% 25: NR All: 1.4%	NR	One death due to lung disorder in Trial 25. 30 randomised patients did not receive BCLT.	See et al.,2002; Iversen et al.,2004; McLeod et al., 2006; Wirth et al., 2007
Urological Associates of Lancaster	RCT, parallel, open-label	Men with prostate cancer (n = 51)	BCLT 150 mg/day	GnRH agonist	3 (5.9%)	1 (2.0%)	NR		Sieber et al.,2004
Derriford Hospital	RCT, parallel, double-blind	Men with prostate cancer (n = 106)	BCLT 150 mg/day + RT	BCLT 150 mg/day + Placebo	NR	1 (0.9%)	NR		Tyrell et al.,2004
CABTPC	RCT, parallel, double-blind	Men with prostate cancer (n = 102)	BCLT 150 mg/day + GnRH agonist	GnRH agonist	14 (13.7%)	2 (2.0%)	NR	“Two patients in the MAB group had a grade 4 ADR relating to hepatic function”	Akaza et al., 2004; Usami et al., 2007

Bristol Urological Institute	RCT, parallel, open-label	Men with prostate cancer (n = 20)	BCLT 50 mg/day + GnRH agonist	CPA 100 mg/day + GnRH agonist	0 (0.0%)	0 (0.0%)	0 (0.0%)		Sugiono et al., 2005
Derriford Hospital	RCT, parallel, open-label	Men with prostate cancer (n = 155)	BCLT 300–600 mg/day	GnRH agonist or Orchiectomy	?	?	NR	“very few patients had clinically relevant changes in liver function”	Tyrell et al., 2006
Memorial Sloan Kettering Cancer Center	NES	Women with ovarian cancer (n = 32)	BCLT 50 mg/day + GnRH agonist	n/a	4 (12.5%)	1 (3.1%)	NR		Levine et al.,2007
BATT	NES	Boys with early onset puberty (n = 14)	BCLT 12.5–100 mg/day + Anastrozole	n/a	1 (7.1%)	0 (0.0%)	NR		Reiter et al., 2010
Taipei National Defense Medical Center	NES	Men with prostate cancer (n = 41)	BCLT 50 mg/day + GnRH agonist	n/a	2 (4.9%)	0 (0.0%)	NR		Kao et al., 2012
SPCETSG	RCT, parallel, open-label	Men with prostate cancer (n = 101)	BCLT 80 mg/day + GnRH agonist	BCLT 80 mg/day + GnRH agonist	18 (17.8%)	2 (2.0%)	NR	Was a comparison of two different GnRHa formulations	Ishizuka et al., 2012
Kindai University	NES	Men with prostate cancer (n = 53)	BCLT 80 mg/day + GnRH agonist + Zoledronic acid	n/a	6 (11.3%)	NR	1 (1.9%)		Nowaza et al., 2013
TBCRC-11	NES	Women with AR+ breast cancer (n = 26)	BCLT 150 mg/day	n/a	7 (26.9%)	1 (3.8%)	NR	Severe (grade 3) liver dysfunction unclear if related to BCLT	Gucalp et al.,2013
SWOG	RCT, parallel, open-label	Men with prostate cancer (n = 104)	BCLT ? mg/day + GnRH agonist	BCLT ? mg/day + GnRH agonist + Cixutumumab	19 (18.2%)	0 (0.0%)	NR		Yu et al., 2015
TERRAIN	RCT, parallel, double-blind	Men with prostate cancer (n = 191)	BCLT 50 mg/day	Enzalutamide	5 (2.6%)	NR	9 (4.7%)		Shore et al., 2016
Princess Margaret Cancer Centre	RCT, parallel, open-label	Men with prostate cancer (n = 26)	BCLT 50 mg/day + GnRH agonist or GnRH antagonist	GnRH antagonist	10 (38.4%)	4 (15.4%)	NR		Sayyid et al., 2017
RTOG	RCT, parallel, double-blind	Men with prostate cancer (n = 382)	BCLT 150 mg/day + RT	Placebo	17 (4.5%)	6 (1.6%)	14 (3.7%)	Life threatening (grade 4) lung toxicity in one patient	Shipley et al., 2017; Struss & Black, 2017
IUHW Mita Hospital	NES	Men and women with AR+ salivary gland cancer (n = 36)	BCLT 80 mg/day + GnRH agonist	n/a	10 (27.8%)	1 (2.8%)	NR	Severe (grade 3) liver dysfunction in one patient attributable to bicalutamide	Fushimi et al., 2018
University of Rome Tor Vergata	RCT, parallel, double-blind	Women with PCOS/hirsutism (n = 28)	BCLT 50 mg/day + OCP	Placebo + OCP	0 (0.0%)	0 (0.0%)	NR	Exclusion criteria were abnormal LFTs	Moretti et al., 2018