

APPENDIX F: PHASE IV SAFETY DATA

Deaths reported in Phase IV studies

Adverse events of special interest in Study A3503 (TELICAST)

DEATHS REPORTED IN PHASE IV STUDIES

*Subject Age	Study Drug	Causal Event	Day of Event	Day of Death	Medical History
4002/12-002/82 y/o	TEL	Carcinoma of the lung	36	48	COPD, Hematemesis
4002/13-002/65 y/o	AZI	Bronchopneumonia, acute exacerbation of COPD	39	47	COPD
4014/1101009/69 y/o	TEL	Suspected pulmonary embolism	2	35	
4014/0204001/62 y/o	TEL	Respiratory failure	114	119	idiopathic cardiomyopathy, hypercholesterolemia
4014/0605003/51 y/o	TEL	Cardiac failure, COPD, Coronary Artery Disease, Pulmonary Heart Disease	164	164	smoking, respiratory insufficiency, heart failure, partial lobectomy for pulmonary disease
4014/0605006/75 y/o	TEL	Pulmonary embolism and left lung cancer	136	147	COPD; bronchitis cough, insomnia, gastroesophageal reflux, depression, left superior lobectomy
4014/0729003/76 y/o	TEL	Cardiorespiratory Arrest, Fatal Cardiac Decompensation	169	182	coronary heart disease, COPD, duodenal ulcer surgery, right aorto-iliac surgery
4014/0909002/88 y/o	TEL	Nosocomial pneumonia	135	144	COPD, alcoholism stopped in 1998, smoking, cholecystitis and gastritis
4014/1201002/88 y/o	TEL	Respiratory failure, pneumonia	22	30	COPD, pneumonia, blow-out fracture of the right orbit (3 Feb 2003 to 30 Mar 2003)
4014/0102016/79 y/o	TEL	Sepsis/urinary tract infection	74	97	pulmonary tuberculosis, COPD, benign prostatic hypertrophy, anxiety
4014/0102024	AZI	Respiratory failure	15	27	
4014/0309006/78 y/o	AZI	Decompensation Cordis due to Cor Senius, Lung Edema	72	93	respiratory insufficiency, lung oedema, urethral stricture, prostatic hypertrophy
4014/1212003/100 y/o	AZI	Heart failure, cardiac arrest	102	102	Chronic bronchitis, COPD, congestive cardiac failure, hypertension
4014/1213004/67 y/o	AZI	Bronchopneumonia, chronic obstructive pulmonary disease, pulmonary embolus	141	141	COPD, hypertension, post-menopausal symptoms, anxiety, hypercholesterolemia

*Subject Age	Study Drug	Causal Event	Day of Event	Day of Death	Medical History
4014/0102014/72 y/o	AZI	Pseudomembranous colitis, sudden cardiac arrest.	139	139	COPD
4014/0104028/77 y/o	AZI	Gastroduodenal ulcer	50	50	Hypertension
4020/140078044/74 y/o	TEL	Fatal brain tumor	49	432	
4020/200176112/81 y/o	TEL	Public highway accident	83	83	Diabetes mellitus, Dyslipidemia, Benign prostatic hypertrophy, Hypertension
4020/2003770155/72 y/o	TEL	Respiratory insufficiency	8	22	Tinnitus, Buccal mycosis
4020/4000475178/54 y/o	TEL	Sudden death	2	2	Emphysema
4020/3003574486/77 y/o	cefuroxime	Bronchus Carcinoma, Metastases to Liver, Lung and Brain	13	24	Cervical Arthrosis, Insomnia, Hypercholesterolemia, Optical Neuropathy, COPD
3502/24040/45 y/o	AMOX/CLA	Pulmonary abscess, Sepsis	1	16	
4015/6010601001/58 y/o	Usual care antibiotic	Respiratory failure, Interstitial pulmonary fibrosis	11	16	

Brief Narratives

Study 4002/AECB

Telithromycin

- Subject no: 12-002: Patient died on Day 48 following initiation of study medication. The patient died of carcinoma of the bronchus.

Azithromycin

- Subject no. 13-002: died on Day 47 from bronchopneumonia.

Study 4014/AECB

Telithromycin

- Subject 1101009: Patient had congestive cardiomyopathy and suspected pulmonary embolism on Day 2, then deep vein thrombosis on Day 17, and died on Day 36.
- Subject 0102016: Patient died 74 days after the first study drug administration, cause of death was sepsis/urinary tract infection.
- Six other deaths in the telithromycin group occurred post-treatment (dates of deaths unspecified), and had the following causes: acute bronchitis (patient no. 0204001); dyspnea, cor pulmonale, and cardiac failure (patient no. 0605003); pulmonary embolism and lung cancer (patient no. 0605006); cardiac failure (patient no. 0729003); cerebrovascular accident and nosocomial pneumonia (patient no. 0909002); and pneumonia (patient no. 1201002).

Azithromycin

- Subject 0102024: Patient had respiratory failure on Day 15 and disseminated tuberculosis on Day 20, he died on Day 27.
- Three other deaths in the azithromycin group occurred post-treatment (dates of deaths unspecified), with the following causes: fatal pulmonary oedema (patient no. 0309006); cardiac arrest (patient no. 1212003); and chronic obstructive pulmonary disease (patient no. 1213004).
- Two additional deaths occurred after the period of observation defined in the study protocol. One death occurred 5 months after first study drug administration (patient no. 0102014); cause of death was sudden cardiac arrest. The other occurred 42 days after the first study drug administration (patient no. 0104028); cause of death was gastroduodenal ulcer.

Study 4020/AECB

Telithromycin

- Subject 2003770155: 71-year old male Caucasian, experienced respiratory failure after completing 5 days of telithromycin treatment.
- Subject 4000475178: Patient, a 54-year old male Caucasian, experienced sudden death on Day 1 of treatment.
- Subject 140078044: Patient developed brain metastases of adenocarcinoma NOS around seven weeks after a 4 day treatment with Telithromycin and more than six weeks after its discontinuation.
- Subject 200176112: Patient was fatally hit by a motor vehicle while walking in the highway more than 11 weeks after Telithromycin treatment.

Cefuroxime

- Subject 3003574486: 77-year old male Caucasian with small cell lung cancer, experienced fatal pneumonia on Day 12 of treatment.

Study 3502/CAP

Amoxicillin–clavulanate

- Subject 24040; Patient suffered an acute respiratory syndrome which resulted in their death.

Study 4015/CAP

Gatifloxacin

- Subject (unspecified) treated with “usual care antibiotics” (gatifloxacin) died from respiratory failure.

ADVERSE EVENTS OF SPECIAL INTEREST IN STUDY A3503

Category/MedDRA preferred term	Telithromycin (N=138) n (%)	Comparator (N=136) n (%)
Visual	3 (2.2%)	0 (0%)
Blurred vision	1 (0.7%)	0 (0%)
Visual acuity reduced	2 (1.4%)	0 (0.0%)
Cardiac	0 (0%)	0 (0%)
Hepatic	2 (1.4%)	0 (0%)
Liver function test abnormal	1 (0.7%)	0 (0%)
Gamma-glutamyl transferase increased	1 (0.7%)	0 (0%)
Blood alkaline phosphatase increased	1 (0.7%)	0 (0%)
Syncope	0 (0%)	0 (0%)

Note: Tables are not additive since one subject may have reported more than one adverse event.