PATTERNS AND OUTCOMES OF INFECTIONS IN PATIENTS WITH LUNG CANCER IN THE CURRENT ERA

MELISSA LUU[1], LINH THI MY NGUYEN[1], JAKE VALENTINE[3,4], ANN OFFICER[5,6], DAVID BALL[3,5], BENJAMIN SOLOMON[3,6], MONICA A SLAVIN[2,3,4], MARLIESE ALEXANDER[1,3] AND BENJAMIN W. TEH[2,3,4]

[1]Pharmacy Department, Peter MacCallum Cancer Centre, Melbourne, Victoria
[2]Department of Infectious Diseases, Peter MacCallum Cancer Centre, Melbourne, Victoria
[3]Sir Peter MacCallum Department of Oncology, University of Melbourne, Parkville, Victoria
[4]National Centre for Infections in Cancer, Peter MacCallum Cancer Centre, Melbourne, Victoria
[5]Department of Radiation Oncology, Peter MacCallum Cancer Centre, Melbourne, Victoria
[6]Department of Medical Oncology, Peter MacCallum Cancer Centre, Melbourne, Victoria, Australia

Peter Mac
Peter MacCallum Cancer Centre
Victoria Australia

Introduction

Infective complications are common in cancer patients, result in serious adverse outcomes, and are a leading cause of death. In regards to lung cancer patients, infection can delay oncological treatment and reduce overall survival[1].

The risk of infection is particularly high for cancer patients receiving chemotherapy due to immunosuppressive effects of these agents. While immunosuppression is typically associated with delivery of cytotoxic agents, there remains a risk of infection and infestations with immune and targeted therapies that are used both as monotherapy and in combination with cytotoxic agents. The risk is mainly due to prolonged neutropenia associated with cytotoxic agents used to treat cancer resulting in higher infection risk caused by invasion of opportunistic pathogens, which can persist after completing chemotherapy treatment[2,3].

Objective

This study reports patterns and outcomes of infection in patients with lung cancer following introduction of immune-based and targeted therapies.

Method

A retrospective cohort study was conducted at Peter MacCallum Cancer Centre spanning 2012 to 2017. Patients were identified from the AUstralian Registry and biObank of thoRAcic cancers (AURORA), a prospective registry that follows the treatment of patients with lung cancer. Admitted episodes of infection were identified through ICD-10-AM codes supplemented by review of clinical and microbiology records.

Data collected included: patient demographics, cancer treatment, episodes of infection and outcomes including intensive care unit (ICU) admission and hospital length-of-stay.

Continuous variables were summarised as median (range) and categorical variables as frequency (percentage). Infection rate was expressed as incidence per 1,000 patient-years. Potential risk factors for microbiologically-defined infections (MDI) were determined using univariate logistic regression modelling.

Table 1: Characteristics of patients with lung cancer hospitalised with infection

Demographic	Number of patients (n=251)	
	No.	%
Age, median (range)	67 (31-91)	
Elderly, % age 70 or older	94	37.5
Sex, % male	150	59.8
Ethnicity		
White	209	83.3
Asian	26	10.4
Other	16	6.4
Performance Status at diagnosis		
ECOG 0-1	196	78.1
ECOG 2-3	52	20.7
ECOG Unknown	3	1.2
Smoking history		
Ever	219	87.3
Past	178	70.9
Current	41	16.3
Never	32	12.7
Pack Years, median (range)	40 (2-165)	
Lung Cancer		
Non-squamous cell	165	65.7
Squamous cell	64	25.5
Small cell	22	8.8
Actionable Mutation (EGFR, ALK, ROS)	37	14.7
PDL1 >=50%	4	1.6
Lung Cancer Stage		
Stage I-II	40	15.9
Stage IIIA	59	23.5
Stage IIIB/IIIC	36	14.3
Stage IV	116	46.2
Cancer treatments during study follow-up*		
No curative or systemic anticancer therapy	33	13.1
Chemotherapy	224	89.2
Immunotherapy	58	23.1
Targeted therapies	87	34.7
Curative chemoradiotherapy	124	49.4
Curative radiotherapy	55	46.2
Curative surgery	116	46.2

*Represents number of patients treated by named modality during study follow-up. Patients treated with multiple treatment lines of the same modality are counted once

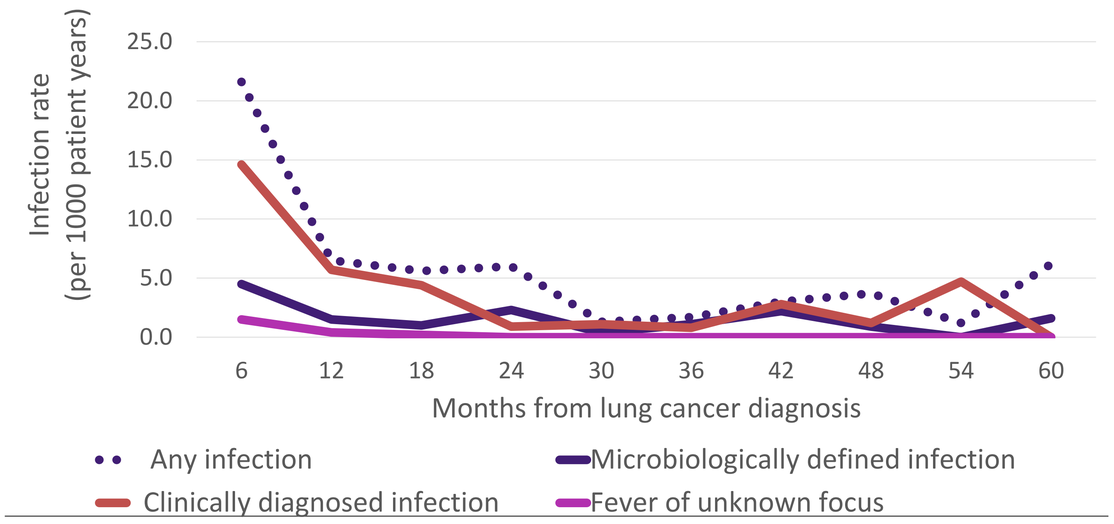

Figure 1: Infection rate with time from cancer diagnosis, by infection category

Results

During follow-up, 251 of 1464 (17.1%) lung cancer patients had 327 infection-related episodes requiring hospital admission. Most patients (59.8%) were male. Median age was 67 years (range 31-91). Majority had non-small cell lung cancer (229, 91.2%) and stage 4 disease at diagnosis (116, 46.2%). Infection rate was the highest in the first 6-months following cancer diagnosis (Figure 1). Over 50% of infection episodes (170/327) occurred during or following systemic treatment; chemoradiotherapy (36.5%; 62/170), conventional chemotherapy (34.7%; 59/170), targeted agents (18.8%; 32/170) and immunotherapy (10.0%; 17/170).

Of 327 infection episodes, 68.5% were clinically diagnosed infections (CDI), 27.2% were MDI and 4.3% were fever of unknown focus (FUF) (Figure 2). Of 89 MDI, 79.8% (71/89) were bacterial, 19.1% (17/89) were viral, and 1.1% (1/89) were fungal infections (Figure 3). Gram-negative bacteria contributed to 57.1% bacterial infections. *E. coli* (18.6%) and *S. aureus* (14.3%) were the most common species isolated. Respiratory syncytial virus (35.3%) was the most common viral pathogen followed by influenza (29.4%). Respiratory tract (69.7%) was the most common site followed by urinary tract (6.7%). Median hospital length-of-stay was 7.2 days and ICU admission rate was 12.2%.

ECOG status ≥2 and small cell lung cancer were associated with increased risk for MDI versus CDI or FUF with OR 2.3 (95%CI: 1.3-3.9, p<0.01) and OR 3.7 (95%CI: 1.9-7.2, p<0.01), respectively. Targeted therapy was associated with lower risk for MDI versus CDI or FUF with an OR 0.3 (95%CI: 0.1-0.8, p=0.02).

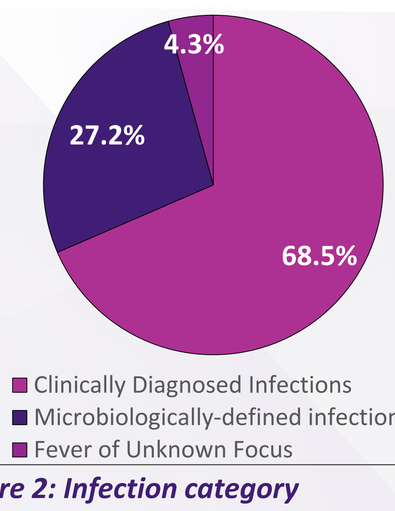

Figure 2: Infection category

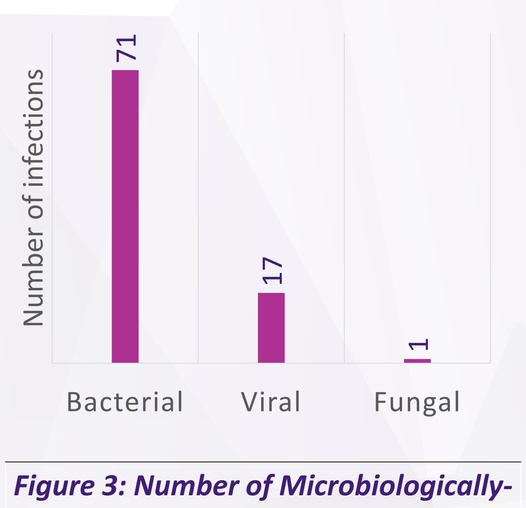

Figure 3: Number of Microbiologically-Defined Infections (MDI)

Conclusions

In patients with lung cancer, a high-risk period (first 6-months of diagnosis) and patient group (ECOG ≥2 and small cell lung cancer) has been identified for potential targeted prevention measures.

Ongoing analyses include evaluation of characteristics and outcomes in this cohort of patients with lung cancer hospitalised with infection, compared with a control group without hospitalisation for infection. Understanding and defining epidemiology and clinical predictors of infection in patients with lung cancer will provide important data to identify patterns and outcomes of care, and periods of increased infective risk, which may be a focus for future improvement initiatives.

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