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Factors associated with lost-to-follow-up status in community pharmacy among Chinese cancer patients using PD-1/PD-L1

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Background

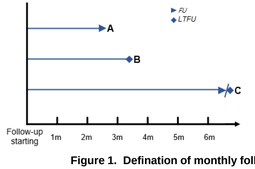
- A variety of PD-1/PD-L1 inhibitors have been widely used in clinical practice in the treatment of cancer.
- Non-compliance with cancer treatment is related to poor clinical outcomes [1-4]. Active patient management services outside hospital may promote disease prognosis [5-6].
- As an important part of patient management and service, community pharmacy could play a key role in the management of cancer patients outside hospital. Study has shown that a two-way communication and feedback program provided by community pharmacies could positively affected adherence outcomes in a chronic myeloid leukemia population [7].

Objectives

- Using data routinely collected from 79 Sipai community pharmacies in China, this study aims to understand the changes of lost-to-follow-up (LTFU) status during the first 6 months after the initial purchase of PD-1/PD-L1 and explore factors associated with LTFU in community pharmacy among cancer patients using PD-1/PD-L1 in China.

Methods

- This is a real-world study using data routinely collected from 79 Sipai community direct-to-patient (DTP) pharmacies during their daily business activities between January 1, 2019 and March 31, 2021 (Purchase/refill data: from January 1, 2019 to January 1, 2021; Follow-up data: from January 1, 2019 to March 31, 2021).
- De-identified records of medication purchase/refill and patient follow-up contacts were extracted from Sipai's data system according to predefined eligibility criteria.
- Date of first follow-up contact after PD-1/PD-L1 initial purchase was defined as the beginning of follow-up; the date of last follow-up contact during the study period was considered as the end of follow-up.
- An individual subject's LTFU status at each time point was determined by her/his duration of follow-up and the LTFU status at the end of follow-up (Figure 1).
- Follow-up response rate (FURR) was defined as the ratio of the number of successful telephone connections during the follow-up period to the total number of follow-up calls during the same period. Follow-up response rate was categorized into three groups, which were high (>70%), middle (30-70%) and low (<30%).
- This study was approved by Shanghai Ethics Committee for Clinical Research (SECCR/2021-104-01).



	LTFU status					
	1m	2m	3m	4m	5m	6m
A	Y	Y	U	U	U	U
B	Y	Y	Y	N	N	N
C	Y	Y	Y	Y	Y	Y
LTFU rate	0		0	B/(B+C)		

Figure 1. Defination of monthly follow-up status and LTFU rate

FU: Follow-up; LTFU: lost-to-follow-up; Y: follow-up; N: lost to follow-up; U: unknown

a) *Patient A: The follow up duration was 2+ months and the status of the last contact record was "follow-up", so the status was "follow-up" in the 1st and 2nd month, and "unknown" in the 3rd to 6th month*
b) *Patient B: The follow up duration was 3+ month and the status of the last contact record was "lost to follow-up", so the status was "follow-up" in the 1st, 2nd and 3rd months, and "lost to follow-up" in the 4th to 6th month*
c) *Patient C: The follow up duration was more than 6 months, so the status was "follow-up" in each month during the first six months of follow-up*

Methods

Eligibility Criteria

- Initial PD-1/PD-L1 purchase was between January 1, 2019 and January 1, 2021.
- Tumor type was not missing in purchase data.
- At least two (≥2) follow-up contacts were recorded in follow-up data.

Statistical Analyses

- Descriptive statistics were used to report baseline characteristics and LTFU rate in the total population and cancer-specific sub-populations.
- Multivariate logistic regression was used to assess the association between LTFU status and predictor variables at different times (1st to 6th month) of follow-up for both total population and cancer-specific sub-populations

Results

- A total of 20,719 subjects met the screening criteria. Considering cancer-specific subgroup analysis, the top 8 tumors(n=16,654) were selected as the final analysis population of this study (Figure 2).
- Of the total study population, 73.15% were men and the median age was 61 years (Table 1).
- The three most common cancer types were lung cancer (53.09%), hepatobiliary cancer (18.63%) and esophagus cancer (9.11%) (Figure 3).
- The overall LTFU rates increased from 7.06% in the first month to 56.54% in the 6th month of follow-up (Figure 4).
- Experiencing adverse events (AE) during treatment was a protecting factor against LTFU (OR<1), and such effect tended to increase as follow-up time prolonged (Figure 5).
- Being enrolled in a patient access program (PAP) showed a protecting effect in the first month of follow-up (OR=0.733, p=0.067), however, it turned to a risk factor in the 2nd month (OR=1.007, p=0.955) and became statistically significant in the 4th month (OR=1.311, p=0.016) and remained constant thereafter (Figure 6).
- Compared with patients with low level follow-up response rate, having middle/high level of FURR were less likely to lose during follow-up (OR < 1 and p<0.05 for all six time points) (Figure 7).

Main cancer-specific sub-populations

- Similar increasing trends of LTFU rate were also observed among three main cancer-specific sub-populations and LTFU rate was lowest in patients with lung cancer (Figure 4).

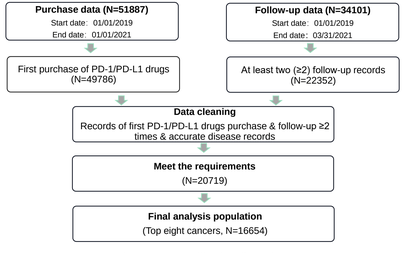
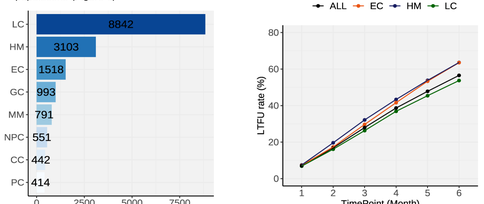


Figure 2. Data filtering flow chart

Results

- The protecting effects of AE and middle/high level of follow-up response rate against LTFU were consistent across different cancer-specific sub-populations in general (Figure 5, Figure 7).
- Although no statistical association was observed between PAP and LTFU in three cancer-specific sub-populations, the effect of PAP on LTFU showed a similar changing pattern among the sub-populations (Figure 6)



LC: Lung Carcer
HM: Hepatobiliary malignancy
EC: Esophageal cancer
GC: Gastric Carcer
MM: Malignant melanoma
NPC: Nasopharyngeal Carcinoma
CC: Cervical Carcer
PC: Pancreatic Cancer

Figure 3. Tumor type distribution

	1	2	3	4	5	6
ALL	7.06	16.86	27.97	38.68	47.82	56.54
EC	7.25	17.32	29.67	41.61	53.34	63.51
HM	7.47	19.63	32.16	43.35	53.82	63.61
LC	6.85	16.11	26.3	36.87	45.41	53.72

Figure 4. LTFU rate in first 6 months among total population and three main cancer-specific sub-populations

Table 1. Demographic and clinical Characteristics of total study population and cancer-specific population

Characteristics	Total (n=16654)	LC (n=8842)	HM (n=3103)	EC (n=1518)
Age, median (Q1,Q3)	61 (53, 68)	62 (55, 68)	57 (49, 65)	63 (57, 69)
Gender, n (%)				
Male	12179 (73.15)	6848 (77.47)	2407 (77.6)	1258 (82.87)
Female	4471 (26.85)	1991 (22.53)	695 (22.4)	260 (17.13)
Patient access program, n (%)				
No	15728 (94.44)	8341 (94.33)	2939 (94.71)	1425 (93.87)
Yes	926 (5.56)	501 (5.67)	164 (5.29)	93 (6.13)
Condition notification, n (%)				
No	3207 (19.26)	1709 (19.33)	600 (19.34)	340 (22.4)
Yes	7905 (47.47)	4155 (46.99)	1556 (50.15)	698 (45.98)
unknown	5542 (33.28)	2978 (33.68)	947 (30.52)	480 (31.62)
AE（%）				
1st	33.5	32.79	37.61	33.93
2nd	37.94	37.04	43.15	38.27
3sd	39.97	38.85	45.41	40.65
4th	41.17	40.31	46.41	41.3
5th	41.84	41.01	47.18	42.16
6th	42.28	41.54	47.47	42.42
Follow-up response rate，n (%)				
High	12746(76.53）	6838(77.34)	2341(75.44)	1183(77.93)
Middle	2851(17.12）	1448(16.38)	560(18.05)	252(16.60)
Low	1057(6.35）	556(6.29）	202(6.51)	83(5.47)

LC: Lung Carer; HM: Hepatobiliary malignancy; EC: Esophageal cancer
Follow-up response rate: number of successful follow-up calls / total number of follow-up calls, >70%(High), 30%-70%(Middle), < 30%(Low)

Limitations

This study was based on the data collected from community pharmacies. Because of the lack of detailed information about disease diagnosis and treatment, the observed results might be biased due to uncontrolled confounders. The collection and recording of all AE related information in this study were based on patients' self-report and pharmacist's personal judgment, which may have the risk of information bias. The association reported in this study does not imply causal relationship.

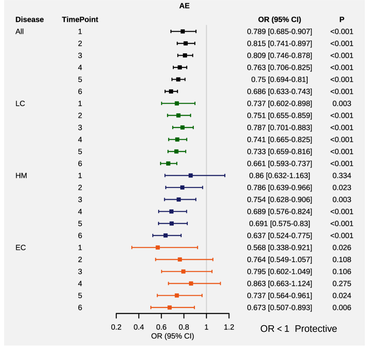


Figure 5. The effect of experiencing AE in first 6 months on LTFU

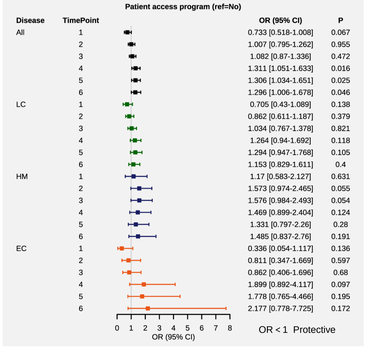


Figure 6. The effect of patient access program in first 6 months on LTFU

Conclusions

More than half of tumor patients who used PD-1/PD-L1 drugs were lost after 6 months of follow-up. Experiencing adverse events and having middle/high level of follow-up response rate were protecting factors against LTFU. High quality follow-up service provided by community pharmacy may play an important role in reducing LTFU among cancer patients using PD-1/PD-L1. Timely adverse event detection and effective management should be the focus of follow-up service at community pharmacy.

Results

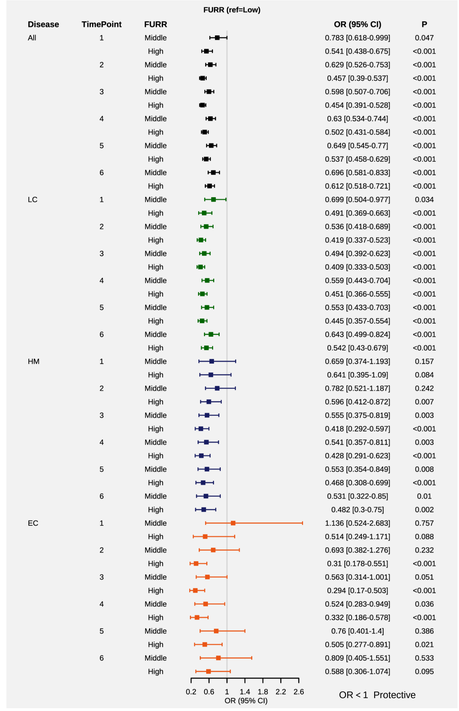


Figure 7. The effect of follow-up response rate in first 6 months on LTFU

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