

# Understanding The Unmet Needs In Diagnosis And Treatment Of Chronic Lymphocytic Leukemia In Korea

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## BACKGROUND

- Chronic lymphocytic leukemia (CLL)** and **small lymphocytic leukemia (SLL)** are the most common leukemias in Western countries but show significant **geographic differences in incidence**.
- While CLL/SLL has an age-standardized incidence rate of 4.75 to 5.4 per 100,000 people in Western and Latin American countries, **East Asia** reports **much lower rates**.
- Interestingly, East Asia has seen the **greatest changes in incidence**, with countries like Korea showing a **4.17% annual percentage change (APC) from 1999 to 2010**.
- The reasons for these differences remain unclear, raising questions about whether CLL/SLL in East Asians has **distinct characteristics**.
- Meanwhile, treatment paradigms for CLL/SLL have evolved, with chemo-immunotherapy previously used for younger patients but now replaced by **targeted therapies** like ibrutinib and venetoclax, which have **significantly improved outcomes**.
- However, challenges such as **adverse effects**, **high costs**, and **resistance to treatment** remain. Fixed-duration therapies and next-generation BTK inhibitors offer promising solutions to these issues.
- Despite these advancements, CLL/SLL remains **incurable**, and the **rising prevalence** of the disease, particularly in Korea, will continue to **strain healthcare resources**.
- This study aims to provide valuable **epidemiological data** to support **future healthcare planning** and **treatment approaches** for CLL/SLL.

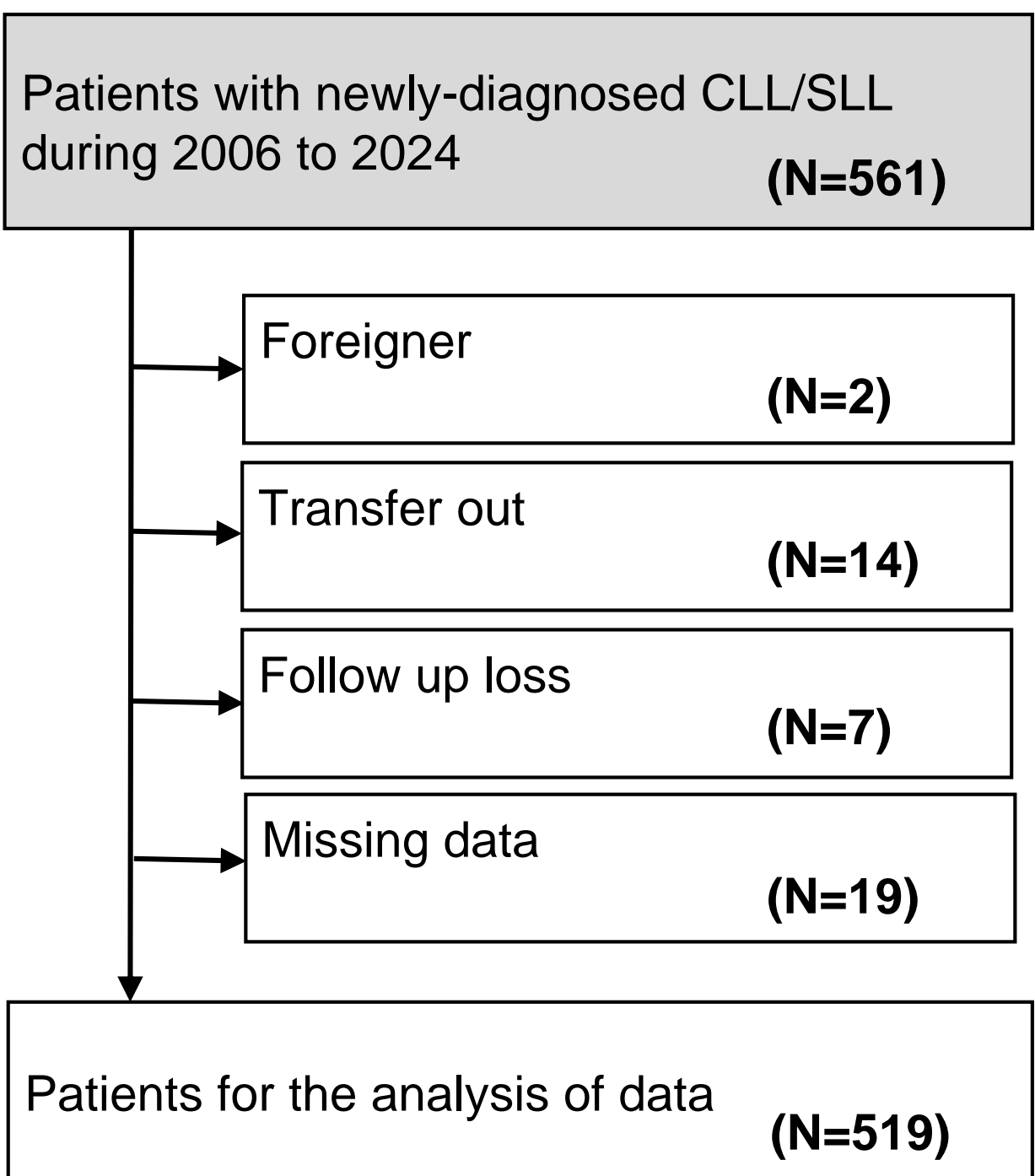
## METHODS

### ❖ Patients

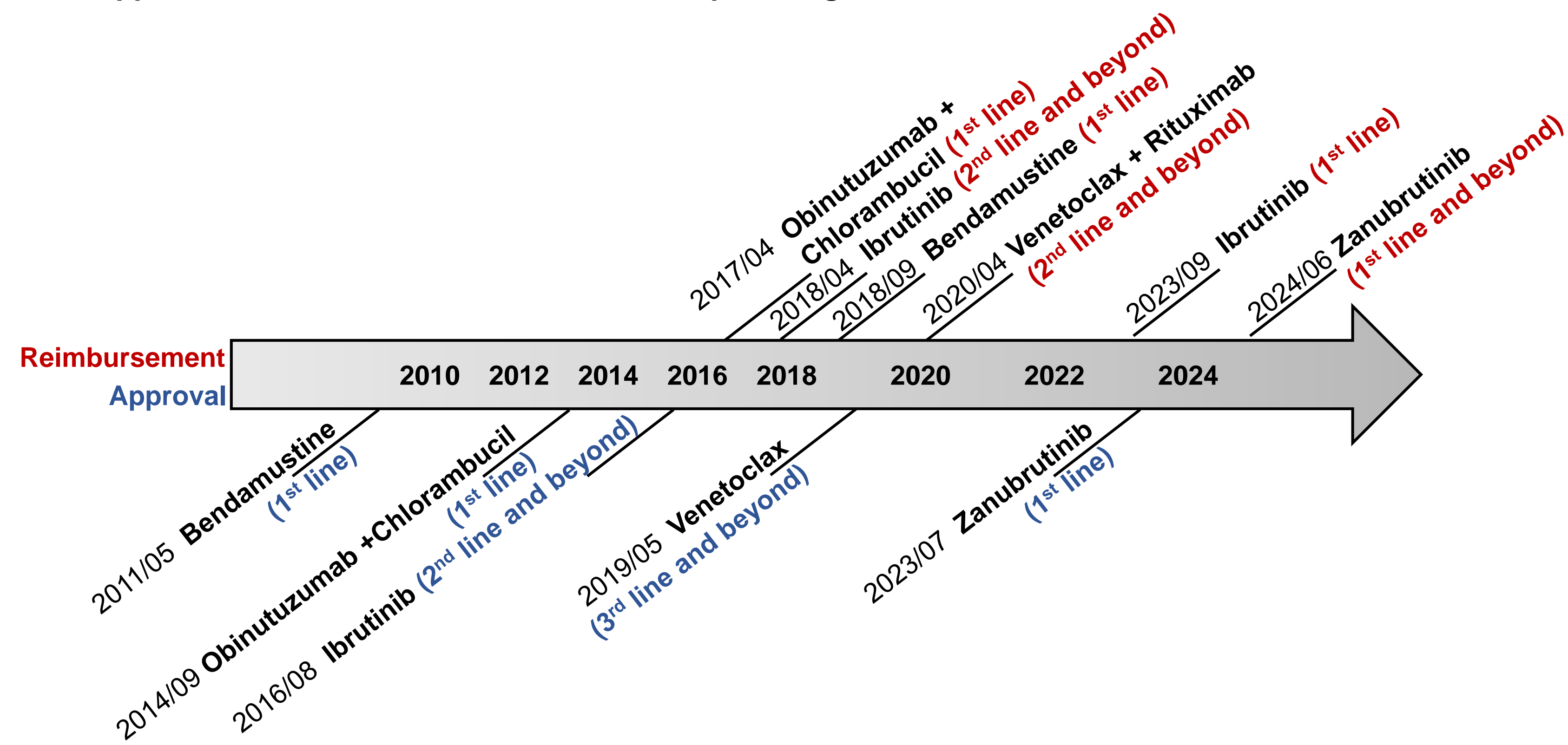
- Multicenter retrospective observational study** involving three major institutions in Korea: Seoul National University Hospital, Catholic Medical Center, and Korea University Guro Hospital.
- Eligible patients were aged ≥18 years and diagnosed with CLL/SLL, as defined by the 2008 International Workshop on Chronic Lymphocytic Leukemia guidelines.

### ❖ Treatment and definitions

- Treatment regimens were classified as follows:
  - immunochemotherapy** (including FCR and obinutuzumab-chlorambucil), **chemotherapy** (which is consisted of only traditional cytotoxic chemotherapy drugs, such as chlorambucil or fludarabine), therapies including **BTK inhibitors** (such as ibrutinib and zanubrutinib) and therapies including anti-apoptotic protein **BCL-2 inhibitor** (Venetoclax).



### ► Approval and reimbursement dates of therapeutic agents for CLL/SLL in South Korea



## RESULTS

### ► Baseline characteristics

Total = 519	N, %
Median age at diagnosis, years	62 (28 - 95)
<65 years	296, 57.0%
65-75 years	157, 30.2%
>75 years	66, 12.7%
Sex, male	317 / 519, 61.0%
Period of diagnosis	
2006-2010	37, 7.1%
2011-2015	120, 23.1%
2016-2020	216, 41.6%
2021-2023	146, 28.1%

CLL-IPI	
Low (0-1)	83, 15.9%
Intermediate (2-3)	87, 16.7%
High (4-6)	38, 7.3%
Very high (7-10)	4, 0.7%
Not available	307, 59.1%

Prognostic variable	
FISH del(17p)	
Positive / Done	9 / 290, 3.1%
Not done	229, 44.1%

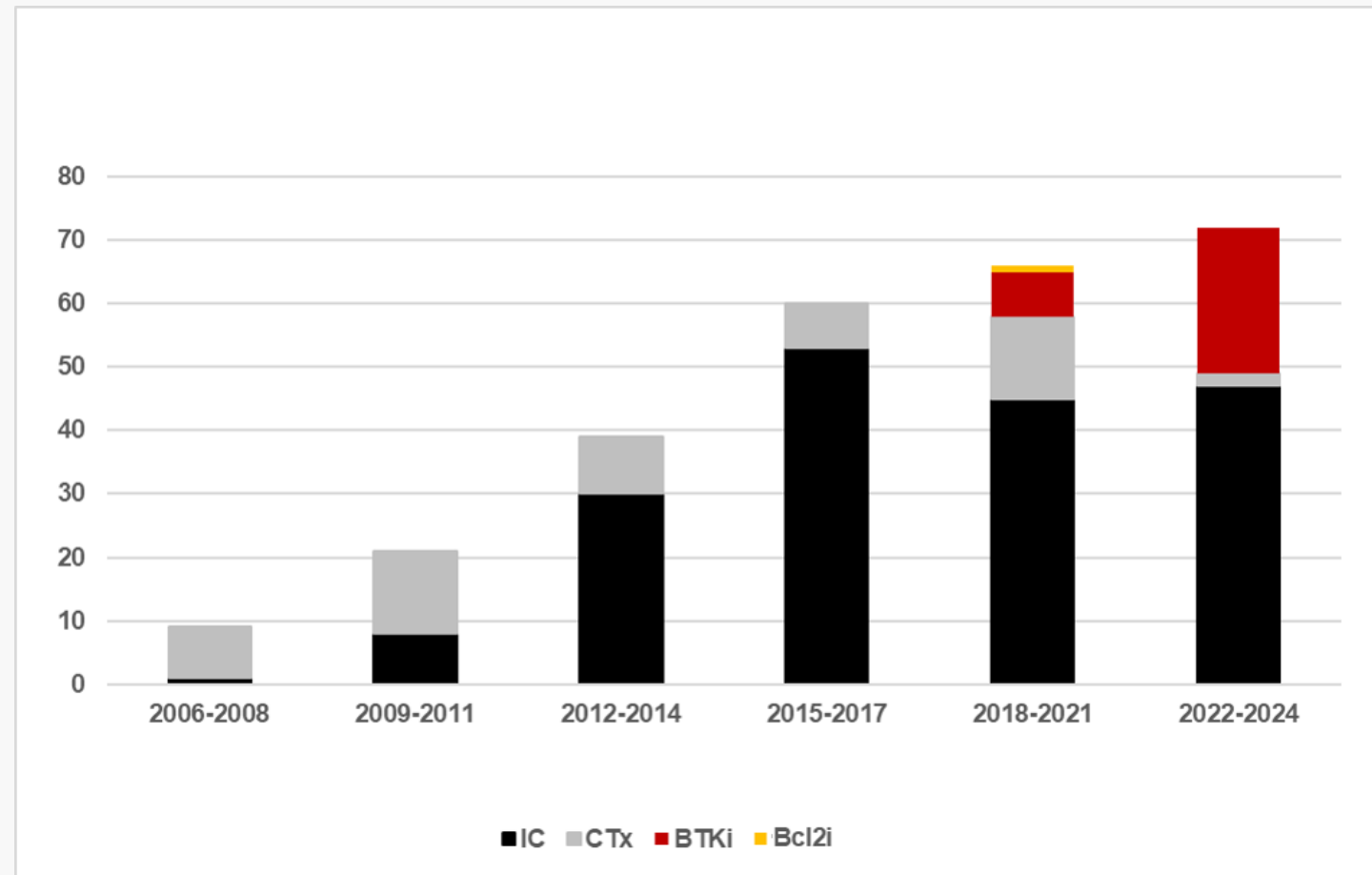
FISH del(13q)	
Positive / Done	103 / 291, 35.3%
Not done	228, 43.9%

DNA sequencing TP53	
Positive / Done	18 / 253, 7.1%
Not done	266, 51.2%

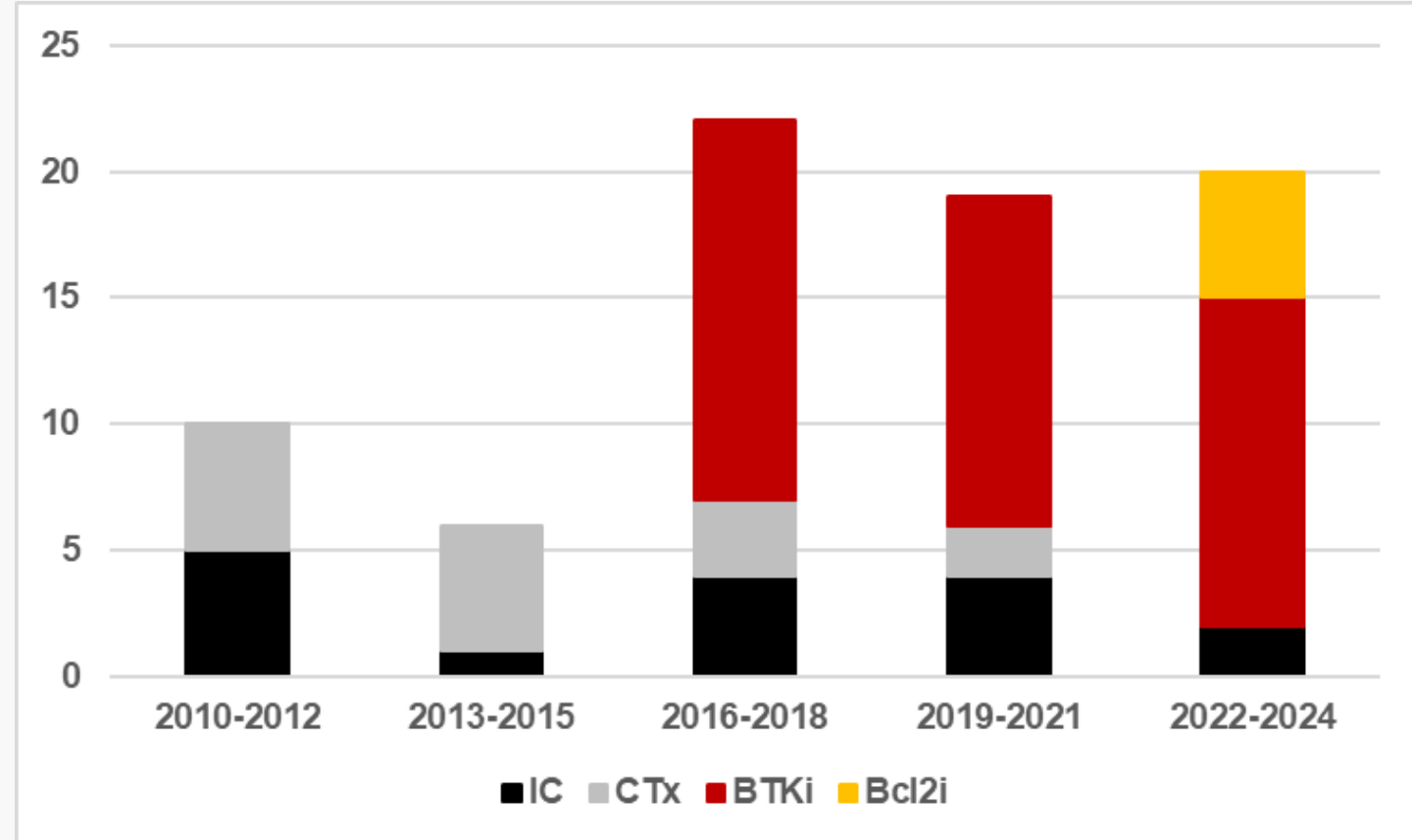
DNA sequencing IGHV	
Positive / Done	10 / 146, 6.8%
Not done	373, 71.8%
Karyotype	
CK / Done	34 / 298, 11.4%
Not done	221, 42.5%

- Immunotherapy** was the most common first-line treatment (68.9%), with FCR accounting for 48.3%, followed by chemotherapy alone (19.4%) and BTK inhibitors (11.2%).
- Since **ibrutinib's approval in 2016**, its first-line use has grown, and it became the **most frequently used second-line** regimen (53.2%), followed by immunotherapy (20.7%) and chemotherapy (19.4%).
- In the third-line setting, immunotherapy (38.0%), BTK inhibitors (23.8%), and BCL2 inhibitor-based regimens (19.0%) were used.
- These patterns reflect **Korea's approval and reimbursement timeline** for CLL/SLL therapies.

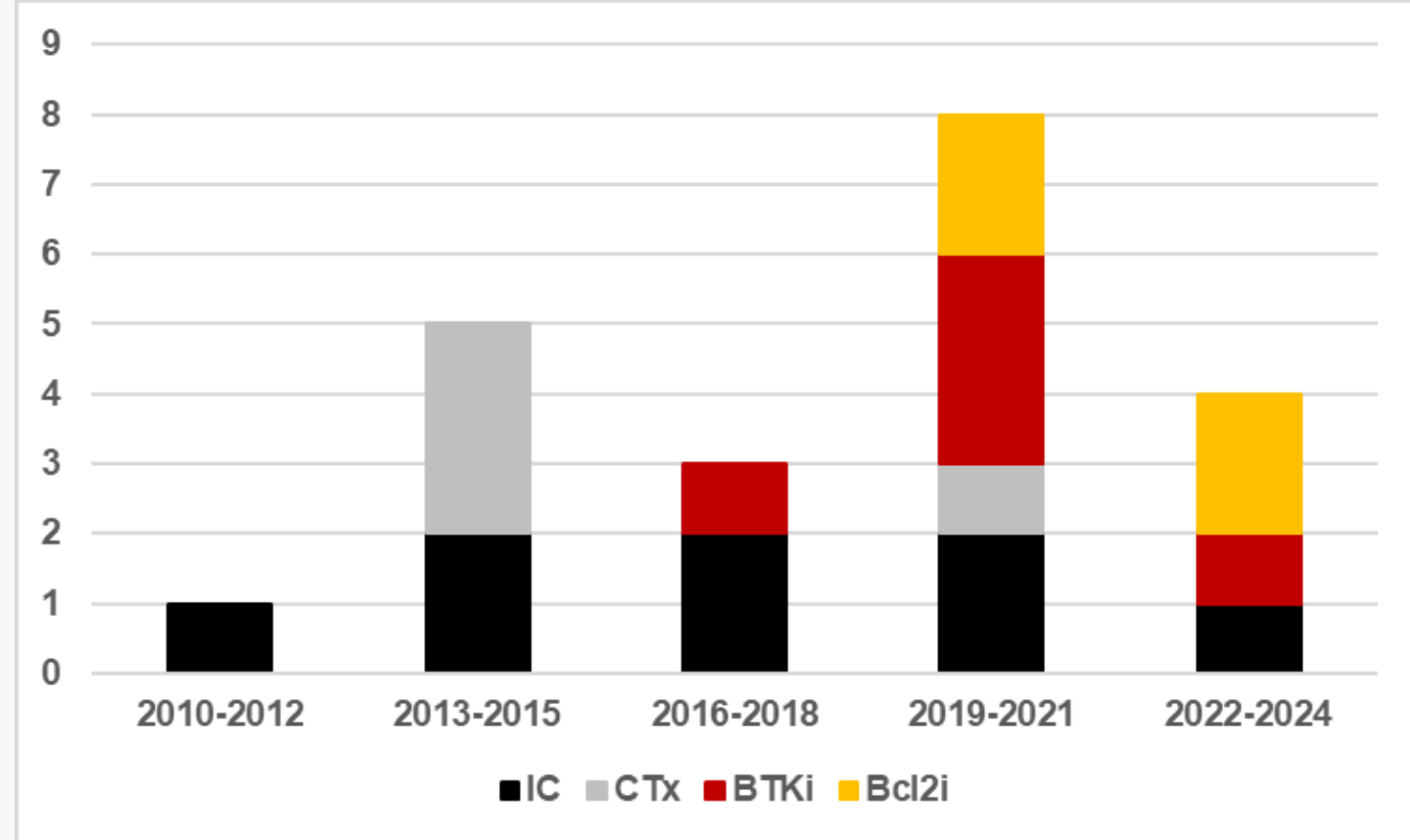
### ► Distribution of treatment regimens by line of therapy



#### ► 1<sup>st</sup> line treatment



#### ► 2<sup>nd</sup> line treatment



#### ► 3<sup>rd</sup> line treatment

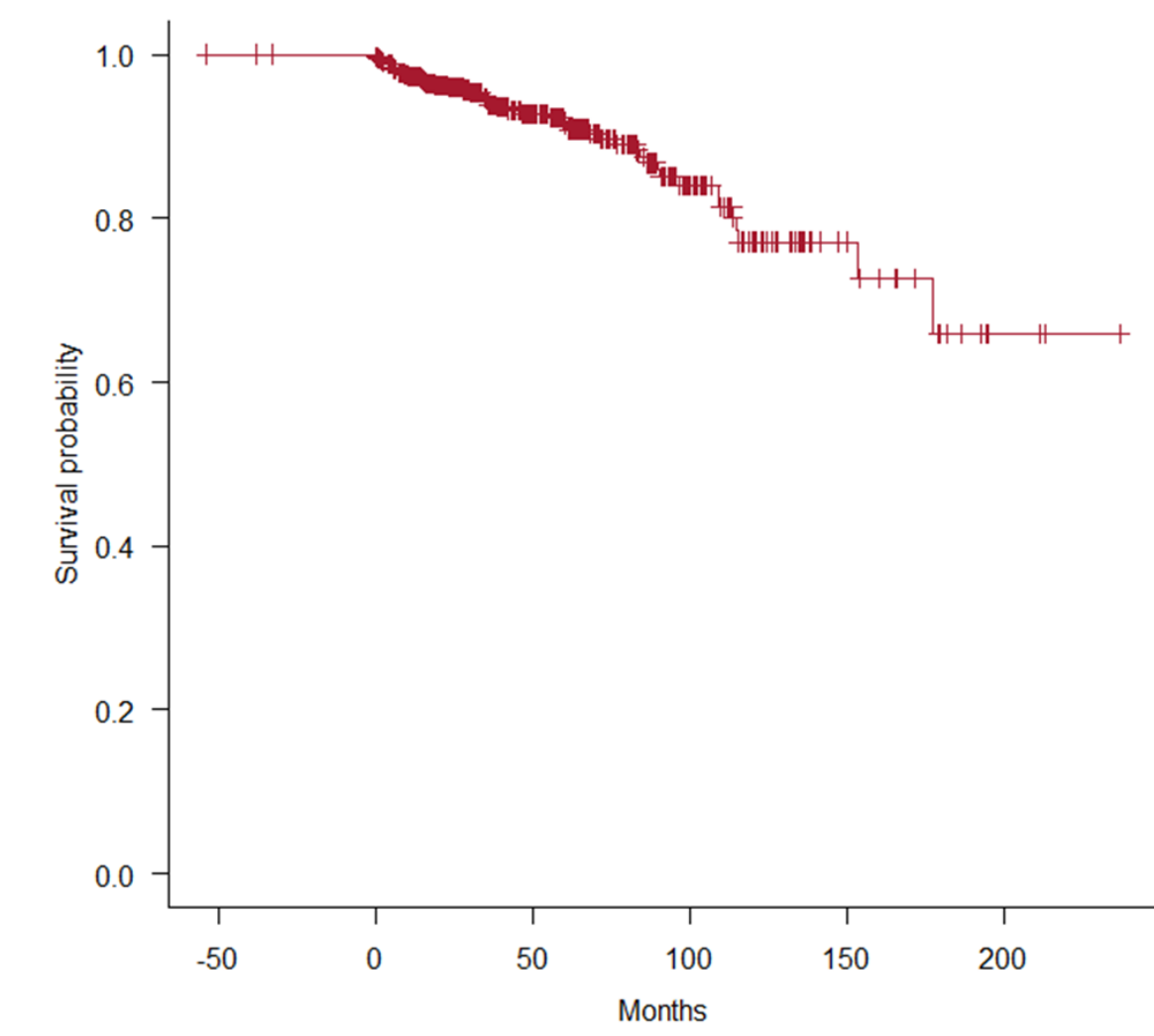
IC, Immunotherapy; CTx, Chemotherapy;

BTKi, BTK inhibitor; Bcl2i, BCL2 inhibitor

- A total of **519 patients** with newly diagnosed CLL/SLL were included in this analysis. The median age at diagnosis was **62 years** (range, 28–95 years). **48.5%** of patients did **not receive any CLL/SLL-directed therapy** during the observation period, whereas **36.6%** received one line of therapy, **10.7%** received two lines, and **4.0%** received three or more lines
- Since ibrutinib's approval in 2016, the use of **BTK inhibitors** has rapidly increased, while immuno-chemotherapy remains common in first- and third-line settings.
- Patients **treated with BTK inhibitors** showed **better survival outcomes** than those receiving immunotherapy, with higher 36-month OS (96.0% vs. 92.0%) and PFS rates (91.8% vs. 80.1%). Prognosis worsened with higher CLL-IPI risk scores, and TP53 mutations were associated with particularly poor outcomes.

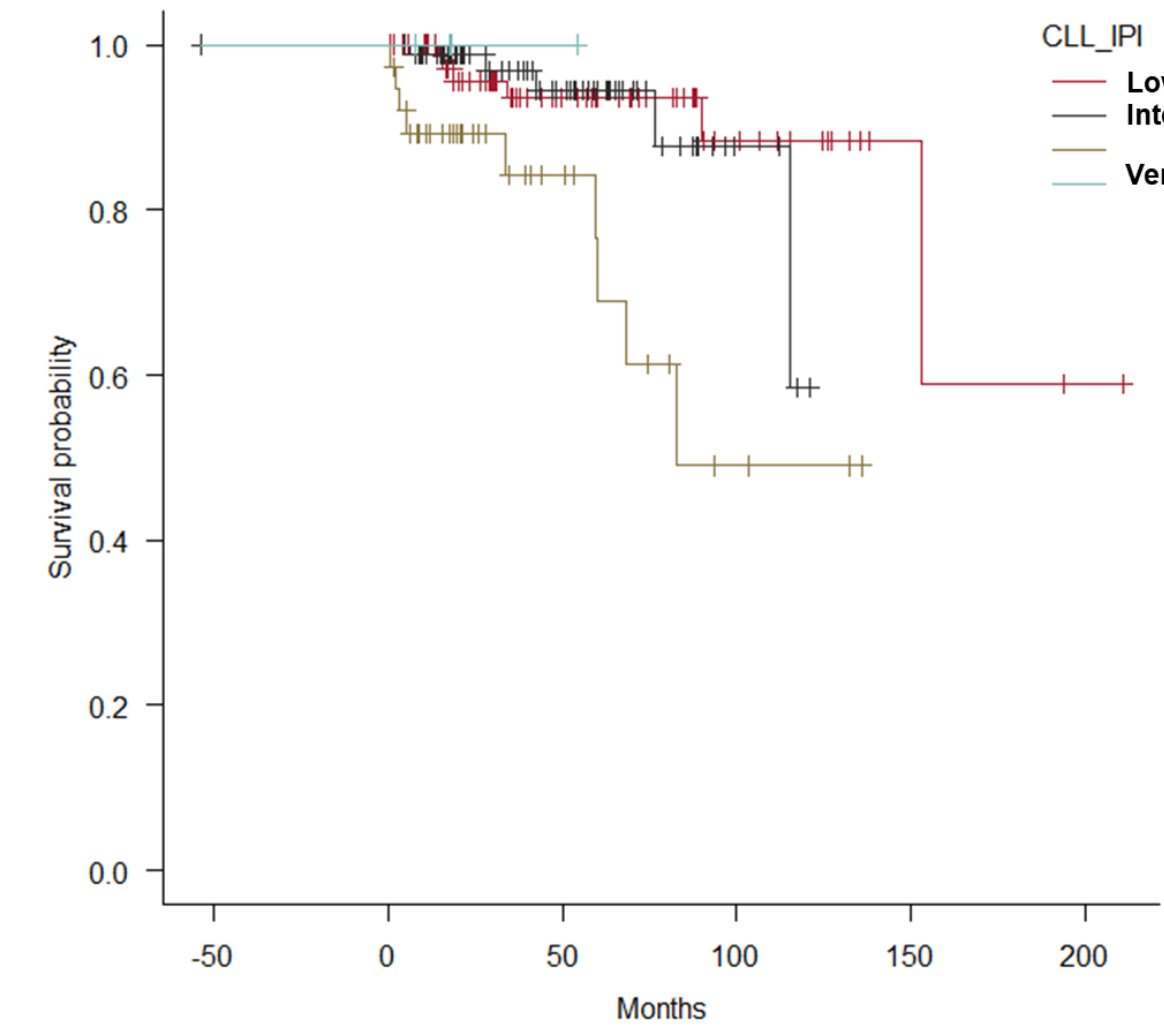
### ► Overall survival

#### ● Total population



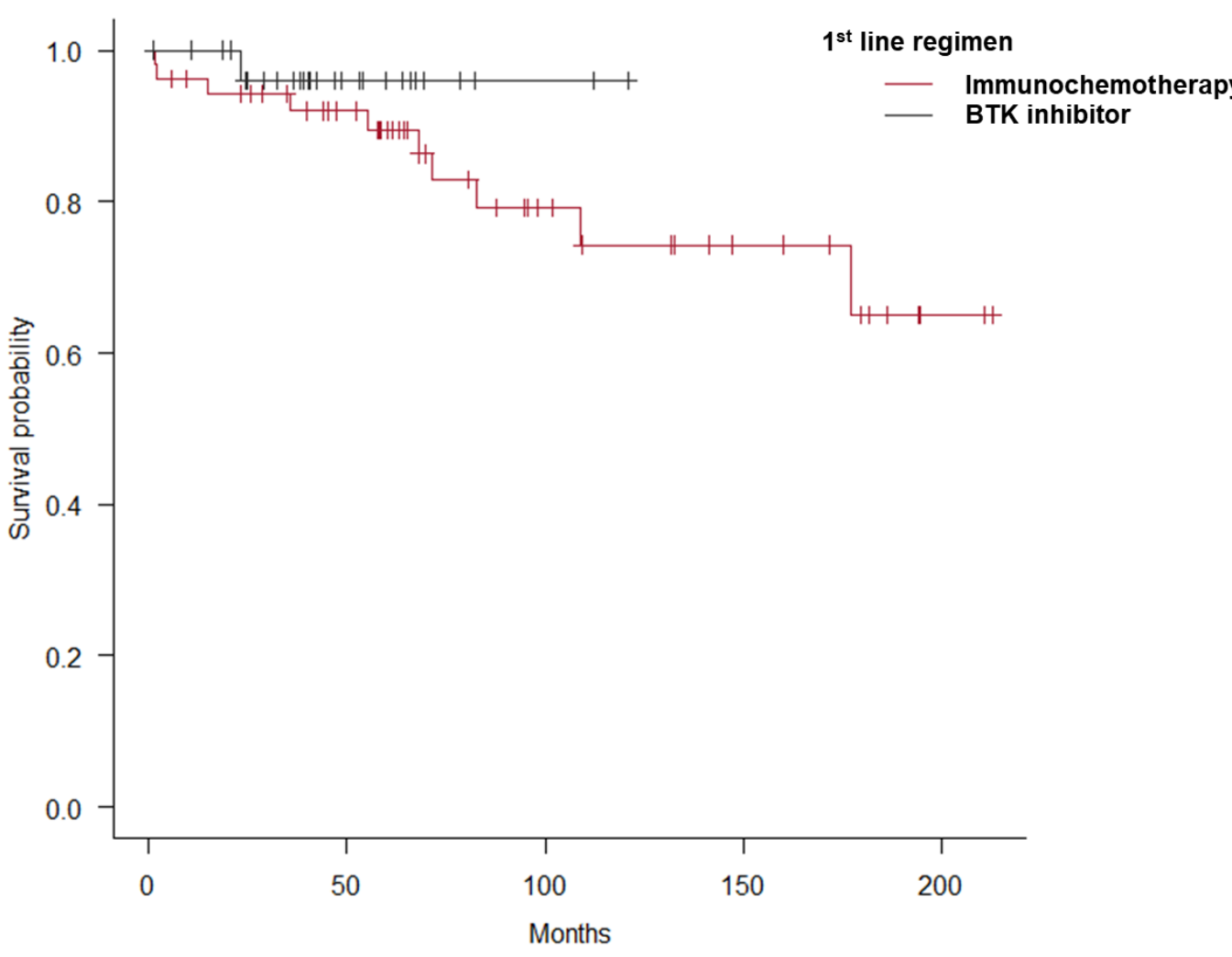
### ► Overall survival by subgroups

#### ● CLL-IPI



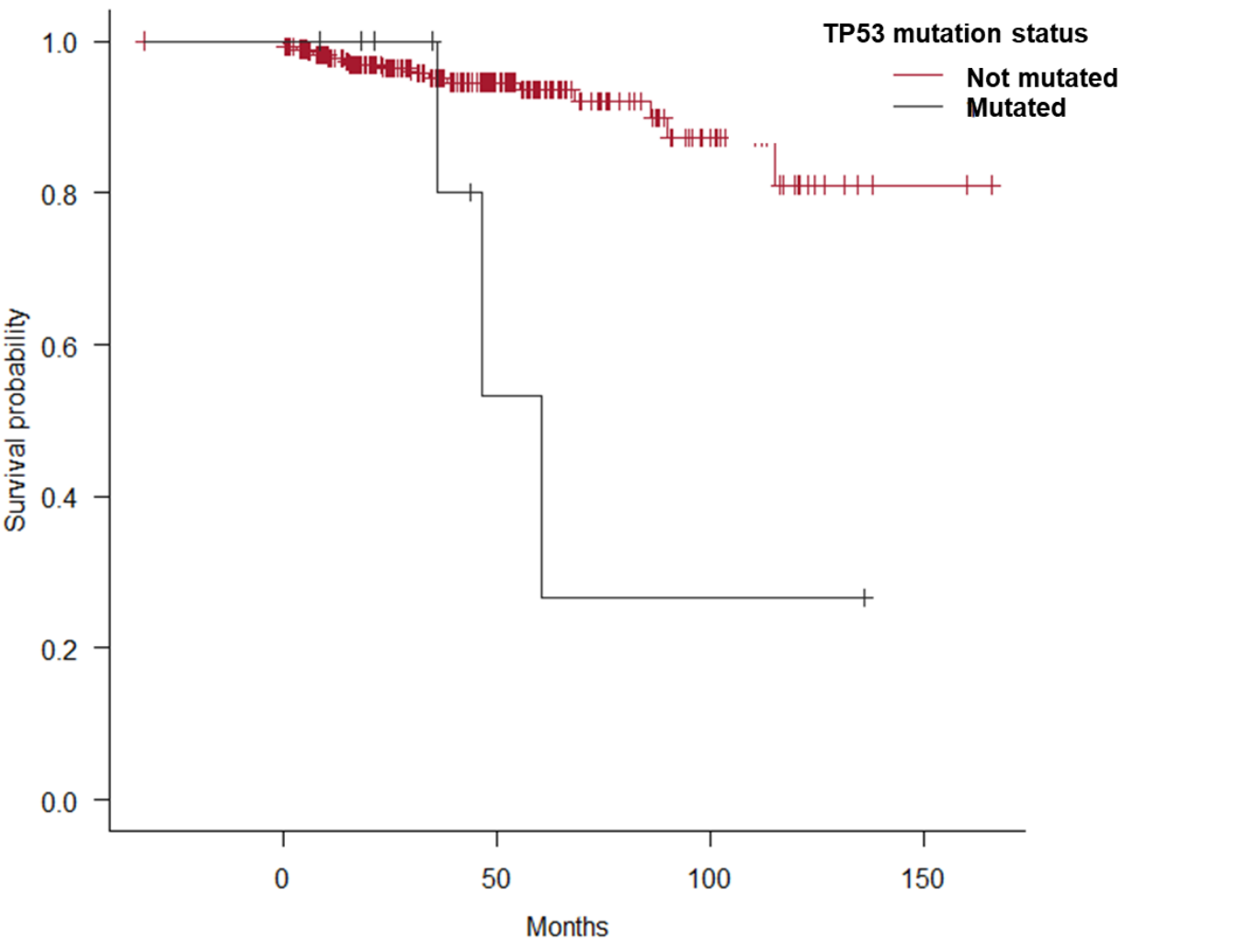
### ► Overall survival by subgroups

#### ● 1<sup>st</sup> line treatment regimen

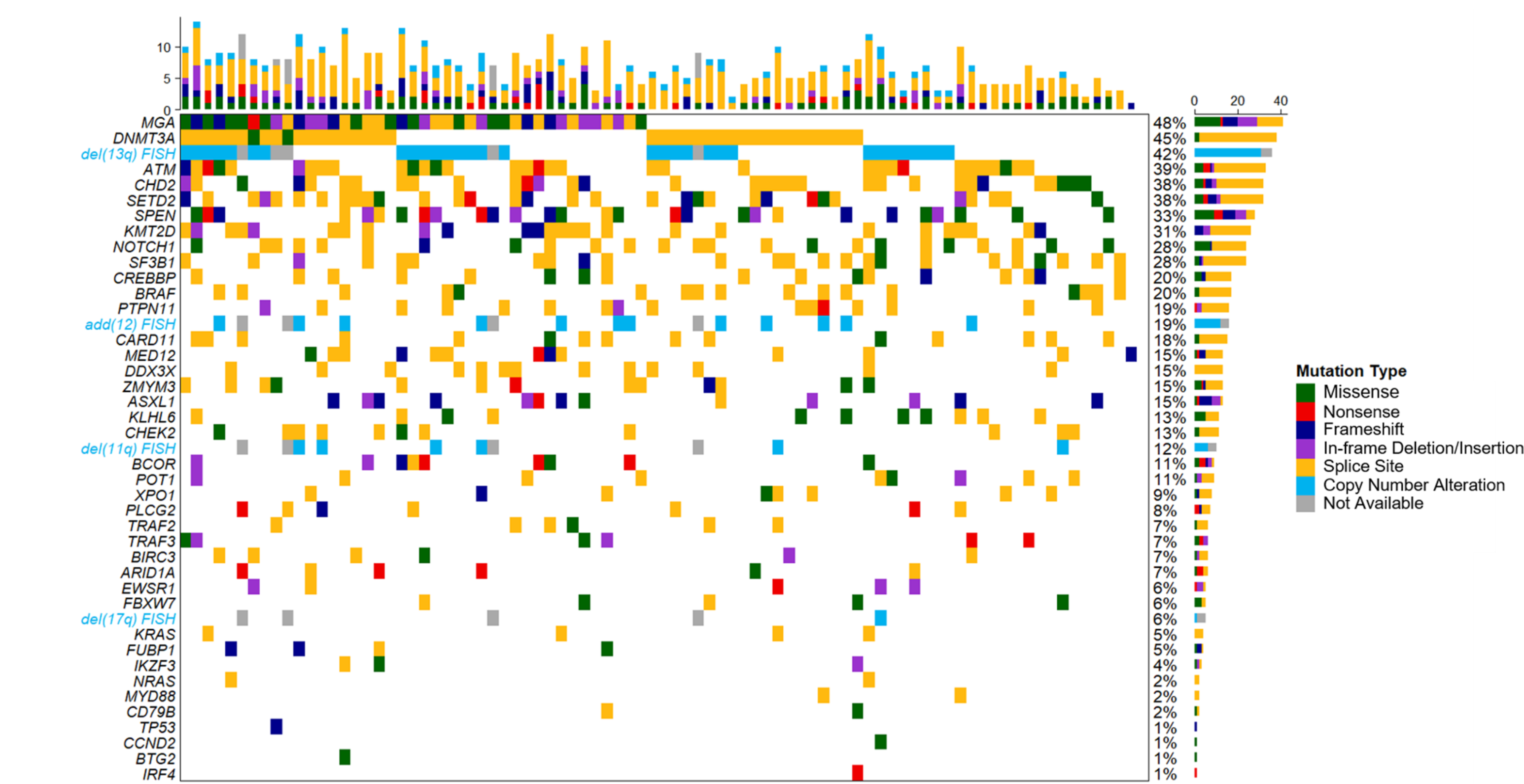


### ► Overall survival by subgroups

#### ● TP53 mutation status



### ► Mutational landscape of 85 CLL patients based on targeted NGS and FISH analysis



## SUMMARIES & CONCLUSIONS

- Compared to real-world cohorts from the other countries, Korean population demonstrated at least a comparable, and often **higher, prevalence of adverse prognostic markers** (e.g., Unmutated IGHV), yet **access to BTK inhibitors** was disproportionately **limited**. Only 11.2% of patients received a BTK inhibitor as first-line therapy.
- Targeted NGS** in a patient subset (n=85) showed mutation frequencies largely consistent with prior domestic studies. Kaplan–Meier analysis of recurrently mutated or well-characterized genes demonstrated survival trends consistent with prior reports, although statistical significance was not reached, likely due to the small cohort size.
- This largest Korean cohort to date provides the most comprehensive real-world picture of CLL/SLL care, laying the groundwork for optimized strategies and policy guidance.