# Real-world treatment and outcome patterns of patients with mantle cell lymphoma in China: a large, multicenter retrospective analysis

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# Abstract

In this study, we aimed to investigate treatment options and the prognosis of patients with mantle cell lymphoma in China. 805 patients diagnosed with MCL between April 1999 and December 2019 at 19 comprehensive hospitals in China were included in this retrospective analysis. The median age of the cohort was 60.0 years with a male-to-female ratio of 3.36:1. 5-year progression free survival (PFS) and overall survival (OS) rates were 30.9% and 65.0% respectively. High-intermediate/high risk group according to MIPI-c, without high-dose cytarabine, lack of Auto-SCT as consolidation and maintenance treatment and SD/PD in initial treatment remained statistically relevant to poor PFS on multivariate analysis (MVA), and ki67 ≥ 50%, B symtoms, high-intermediate/high risk group according to MIPI-c ,without high-dose cytarabine ,lack of maintenance treatment ,SD/PD in initial treatment and relapse/refractory state were independently associated with poorer OS on MVA. First-line high dose cytarabine exposure, auto-SCT as consolidation therapy obtained survival benefits in Chinese population. and our study further confirmed the value of maintenance treatment and explored the application of new drug treatment and bendamustine in R/R MCL patients.


# Introduction

Mantle cell lymphoma (MCL) is an uncommon heterogeneous subtype of B cell non-Hodgkin lymphoma, which is characterized by overexpression of cyclin D1 as a result of translocation t (11;14) (q13;q32). MCL comprises 3–10% of non-Hodgkin lymphomas in Western countries(1–5). The median age at diagnosis is about 68 years and predominantly occurs in male patients with the ratio of 3:1(4, 6). Despite the heterogeneity of clinical behaviors and prognosis, most MCL cases have a rapid evolution and an aggressive behavior with an unfavorable outcome(7). Median overall survival (OS) following initial induction therapy is 3–5 years with the use of dose-intense chemotherapy or combination therapy, incorporation of anti-lymphoma antibodies, and autologous stem cell transplantation. Patients with refractory and relapsed disease often respond poorly to chemotherapy and progress rapidly, resulting in the median overall survival of 1–2 years(8).

Clinical features in mantle cell lymphoma appeared regional characteristics. The median age of onset was 59–60 years in Asian, which was lower than that reported in European and American countries(9, 10). The epidemiology of MCL in Asia is not accurate documented but appears to comprise 2–6% of all lymphoma in different countries. In China, small sample sizes show that the incidence rate varies from 2.6%-6.3%(11–13). With the standardization of treatment and diagnosis, especially the extensive use of immunohistochemical markers such as CyclinD1 and Sox11 in the diagnosis of MCL, it is significant helpful to discriminate from other B cell lymphomas. Therefore, the diagnosis rate and incidence rate of mantle cell lymphoma have increased in recent years. Although there is no standard guidelines for MCL, the recognized treatment options in young fit patients are that aggressive chemo-immunotherapy containing high-dose cytarabine combined with autologous hematopoietic stem cell transplantation as the consolidation therapy and rituximab as maintenance therapy. For older patients, it is most commonly used chemo-immunotherapy and rituximab maintenance(9, 10, 14–17). However, in the real world, MCL

treatment opinions are not uniform between country/region within Asia and China and Asian patient-specific data for the treatment of MCL are lacking.

As the above background, to address the knowledge gap in Chinese MCL patients, we present data from an analysis based on a multicenter 20-year retrospective registry. In this study, we focus on the clinical characteristics, treatment patterns and prognosis of MCL patients in China.

# Materials And Methods

### Patients

Patients diagnosed with MCL between April 1999 and December 2019 at 19 comprehensive hospitals in China were included in this retrospective analysis. The median follow-up duration was 36.0 months. The data of total 805 patients with mantle cell lymphoma were collected, 112 patients with incomplete clinical data, no chemotherapy, and missing follow-up data were excluded. Finally, 693 patients with complete clinical data and survival follow-up data were included in survival analysis(Figure1). Diagnostic specimens underwent the pathological review according to World Health Organization criteria. Medical records were reviewed for demographic and clinical data. The data including baseline clinical features, physical examinations, biological data, treatment, and survival were collected. The above medical records and study protocol conformed to the ethical requirements of Peking University Third Hospital. The study was performed in accordance with the ethical standards of Helsinki and its later amendments.

### Data Collection

Clinical characteristics included sex, age, the presence of B-symptoms, Eastern Cooperative Oncology Group (ECOG) performance status, Ann Arbor staging, extranodal disease, blastoid or pleomorphic morphology, Ki-67 index, blood counts, LDH levels, β2 microglobulin levels. Treatment information was also collected for analysis, including first-line chemotherapy, autologous stem cell transplantation (ASCT), maintenance treatment, and treatment options of relapsed/refractory MCL. Risk stratification is mainly based on MIPI score and MIPI-c score, which were calculated with sufficient data as previously published.

### Statistical Analysis

OS was defined as the date from diagnosis MCL to the date of death from any cause or was censored at the date of last follow up for survivors. PFS was calculated as the time elapsed between the date of diagnosis to the date of relapse, progression, or death from any cause. Fisher’s exact test or Pearson’s Chi-squared test were used to compare categorical variables, as appropriate. PFS and OS was estimated according to the Kaplan-Meier survival method. By using univariable and multivariable Cox regression models, comparisons between the variables of interest were conducted. The log-rank test was then used to determine hazard ratios (HR), the corresponding 95% confidence intervals (95% CI) of mortality and the p-values. Only variables with a certain significance ($p < 0.05$) in the univariable analysis were included in

the multivariable model. P level of 0.05 was considered statistically significant. All outputs were produced using R version 4.1.0.

# Results

### Clinical and demographic characteristics

A total of 693 mantle cell lymphoma patients with integrated clinical, treatment, and follow-up data from 19 centers in China were included in this study. 534 patients were male (77.1%), with a male-to-female ratio of 3.36:1. The median age at diagnosis was 60.0 years (range, 25-88 years). Four hundred and seventy-eight patients (69.0%) were younger than 65 years at diagnosis, and two hundred and fifteen patients (31.0 %) were older than 65 years. Clinical and demographic characteristics of the younger and older patients are summarized in Table 1. Compared with the younger cohort, older patients were more likely to have extranodal organs(P=0.003), bone marrow involvement(P=0.004), and high level of LDH (P=0.044). According to MIPI and MIPI-c prognostic scoring index, the proportion of high-risk group and high/high-intermediate risk group in elderly patients is more higher, 33.5% vs 11.3% and 58.2% vs 28.5%, respectively.

At the same time, we collected the clinical manifestations of patients at diagnosis. The main symptoms were as follows: superficial tumor or mass (62.6%), abdominal pain or distension (14.1%), dysphagia (7.8%); the secondly symptoms were fatigue, fever, abnormal hemogram, and hepatosplenomegaly.

### First-line and maintenance treatment

In our study, all 693 patients received chemotherapy as first-line treatment. The therapeutic schedule is not completely unified. Among of them, the most frequently regimen is CHOP/CHOP-like±R with 312 patients(45.0%) used, 222 patients（32.0%）were treated with high-dose cytarabine, 154 patients(22.2%) received CHOP / DHAP±R regimen, and 45 patients (6.5%) received dose adjusted hyper CVAD±R regimen, and 23 patients (3.3%) received  high cytarabine + R regimen , 44 patients (6.3%) received VR-CAP regimen,30 patients (4.3%) received BR regimen, 55 patients(7.9%) initially chose chemo-free regimen including IR / R2 / IR2,and other less used initial treatments included R-EPOCH (n = 17, 2.5%) and FC / FCM±R regimen (n = 13, 1.9%)(Figure2). Despite the high proportion of young patients, only 80 patients (11.5%) received autologous hematopoietic stem cell transplantation as consolidation therapy after chemotherapy remission.

In this study, 309 patients (44.6%) received maintenance therapy as consolidation treatment after initial treatment. Among them, 151 patients (21.8%) received rituximab maintenance regimen, 43 patients (6.2%) received lenalidomide maintenance regimen, 47 patients (6.8%) received ibrutinib maintenance therapy, and 67 patients (9.7%) received IR / R2 regimen as the maintenance therapy.

### Response data and relapse/refractory treatment

In the initial treatment, the overall response rate (ORR) was 85.0%, of which complete remission (CR) rate was 46.6%, partial remission (PR) was 38.4%. Furthermore, the study compared the efficiency between different first-line treatment regimens. The results showed that the ORR rate and CR rate in high-dose cytarabine regimen were better than other non high-intensity treatment regimens, 92.4% vs 81.5% and 68.6% vs 36.2%, respectively. There was statistical difference between the two groups (P=0.000, P=0.000).

In the follow-up time, 409 (59.0%) patients were relapsed and refractory, of which 104 patients (15.0%) were refractory, 305 patients (44.0%) relapsed after remission. We further analyzed the correlation between clinical parameters and whether patients were relapsed and refractory. Binary logistic regression analysis showed that age≥65 years old, stage III /IV by Ann Abor staging, B symptoms, high-risk group according to MIPI-c and MIPI index, elevated LDH level and initial treatment without high-dose Ara C and without maintenance treatment were the related factors to replased/refractory in MCL patients. Multiple logistic regression analysis suggested that elevated LDH level and initial treatment without high-dose Ara C and without maintenance treatment were independent related factors in relapse/refractory MCL.

Among them, 360 available patients received treatment including salvage chemotherapy, new drug therapy and BR regimen chemotherapy. The new drugs mainly included lenalidomide, ibrutinib and bortezomib, which are used alone or in combination with other drugs.125 patients only received salvage chemotherapy, the ORR was 29.6 % and CR was 7.2%. 205 patients received new drugs single or combined treatment with ORR 64.4% and CR16.1%. 30 patients were treated with BR regimen, and the ORR was 53.3% and CR was 23.3% respectively.

### Survival and prognostic factors

During the follow-up to June 2021, 222 patients (32.0%) had died. The 3-year and 5-year PFS of the global series was 51.5% and 30.9 %the 3-year and 5-year OS of the global series was 78.6% and 65.0 %, respectively (Figure3). In univariable analysis, we analyzed the common variables, which including age, gender, tumor proliferation index, pathological type, stage, B symptoms, LDH level, ECOG, extranodal organ involvement, different extranodal involvement sites, MIPI index, and MIPI-c index. At the same time, we also analyzed the treatment related factors, including initial treatment regimens, autologous hematopoietic stem cell transplantation, initial therapeutic efficacy, relapsed/refractory and treatment lines.

The result showed that age ≥ 65 years, ki67≥30%, ki67≥50%, stage -, B symptoms, LDH elevated, extranodal organ involvement, spleen involvement, bone marrow involvement, high-risk group according to MIPI/MIPI-c index, high-dose cytarabine in first-line therapy, auto-ASCT, maintenance treatment, CR/PR in initial treatment were significantly correlated with worse PFS in univariable analysis. Except of the above factors ,year of diagnosis, pathological subtype and relapsed/ refractory state were associated with poor OS in univariable analysis.

Low-intermediate/low risk group according to MIPI-c, high-dose cytarabine regimen, auto-ASCT as consolidation therapy, CR/PR after initial treatment and maintenance treatment were associated with better PFS on multivariable analyses (Table2, Figure4). Meanwhile, ki67≥50%,B symtoms, high-intermediate/high risk group according to MIPI-c, without high-dose cytarabine, lack of maintenance treatment, CR/PR after initial treatment and relapse/refractory state were the independent prognostic factors for OS (Table2, Figure4).

In our cohort, we compared PFS and OS according to different induction regimens. There were significant differences in PFS and OS between high-dose cytarabine-containing regimen group and non-intensified chemotherapy group, and the 5 year-PFS and OS were 48.9% vs 24.0% and 81.7% vs 57.0%, respectively ($p<0.001$, $p<0.001$, Figure5). Among the young patients, 191 patients chose the treatment regimen containing high-dose cytarabine in the initial treatment. As the same as the overall population, the high-dose cytarabine treatment group has the survival advantage in the young cohort, with the 5 year-PFS and OS were 50.4% vs 27.3% and 83.2% vs 67.5%, respectively ($p<0.001$, $p<0.001$, Figure5). Further, we compared the different cytarabine-containing regimens in the young cohort, 122 young patients received CHOP / DHAP±R regimen, and 42 patients received dose adjusted hyper CVAD±R regimen, and 22 patients received R- high cytarabine regimen. There was no significant difference in PFS and OS between different high-dose cytarabine regimens ($p=0.144$, $p=0.494$ , Figure5).

55 patients (7.9%) initially chose chemo-free regimen including IR / R2 / IR2 due to unfit condition or refusing chemotherapy, the ORR rate and CR rate were 81.8% and 23.6% in this group, the 5-year PFS and 5-year OS was 34.5% and 57.1%, respectively. There was no significant difference in PFS compared with chemo-regimens ($p=0.359$), however, chemo-regimens was better than chemo-free group in OS($p=0.003$), which may due to the unfit state and short follow-up time in chemo-free cohort.

Survival was compared in patients who were treated with Auto-SCT (N=80) and non-ASCT as consolidation therapy (Figure6). 5-year PFS rates were 68.8% vs 25.3% ($p<0.001$) and 5-year OS rates were 87.3 %vs 61.7% ($p<0.001$) respectively. We further compared PFS and OS according to induction regimens with or without Auto-SCT. Non-intensified induction regimens with Auto-SCT(N=29) , and without Auto-SCT(N=441), 5 -year PFS and 5-year OS rates were 66.0% vs 20.3%(($p<0.001$), 78.1% vs 55.4% ($p=0.012$) respectively(Figure6). In high-dose cytarabine induction regimens with Auto-SCT(N=51) and without Auto-SCT (N=172) groups, 5-year PFS and 5-year OS rates were 68.5% vs 42.1%($p=0.004$), 90.4% vs 78.8% ($p=0.11$) respectively (Figure6).

Maintenance regimen in our research was not consistent. Once again, we further compared PFS and OS with or without MR. The 5-years PFS and 5-years OS rates in the maintenance regimen and non-maintenance regimen group were 53.6 % vs 17.2% ,82.7% vs 52.9% respectively. There were significant differences between the two groups ($p<0.001$, $p<0.001$). However, there was no significant difference in PFS and OS between different maintenance therapy including rituximab, lenalidomide, ibrutinib and IR/R2 regimens ($p=0.520$ $p=0.270$) (Figure 7).

The Kaplan–Meier method was applied to estimate time-to-event outcomes (OS-2 and comparisons between treatment groups were performed in our cohort. Compared with salvage chemotherapy, new drugs treatment and BR regimen have obvious survival advantages and the median OS-2 for patients with new drugs treatment and BR regimen were 21.0 months and 23.0 months respectively, the median OS-2 of patients treated with salvage chemotherapy was 16.0m ($p<0.001$ ,Figure 7).

### Second neoplasms

During the follow-up of this study, 34 patients (4.90%) complicated with or developed a secondary malignancy. The most common secondary malignancy is lung cancer (N=7), the second is hematological malignancies, including AML, ALL, MDS and DLBCL(N=6), then followed by breast cancer(N=4), prostate cancer(N=3) gastric cancer (N=3) and colon cancer (N=3). (Table3)

## Discussion

Mantle cell lymphoma is a rare B cell lymphoma that is described as an aggressive, generally incurable lymphoma with formerly poor long-term survival(1–3). Previous reports have shown that the incidence rate of mantle cell lymphoma in Asia is significantly lower than that in western countries(9, 10). Based on the observational database research study, MCL accounts for approximately 3% of malignant lymphoma in Japan(18).To the best of our knowledge, this is the largest retrospective study limited to MCL in Chinese population. In terms of demographic characteristics, the number of patients in this study increased significantly after 2015, which was mainly related to the improvement in diagnostic level, especially the immunohistochemical markers of CyclinD1 and Sox11 that were used as routine examinations for the diagnosis of B-cell lymphoma in large hospitals in China. MCL often occurs in male patients in the Asian population, and the median age at initial presentation is 60 years, which is significantly lower than that in Western and American countries. In pathological subtypes, compared with previous reports, 10–15% of patients present with a more indolent subtype, non-nodular mantle cell lymphoma only accounted for 3.3% in our corhort and the majority of these patients have symptoms and treatment indications(19). Most newly diagnosed patients display aggressive disease features, blastic/pleomorphic mantle cell lymphoma accounted for 12.8%, ki-67 ≥ 30% was 57.7% and ki-67 ≥ 50% was 26.1%. Meanwhile, the proportion of extranodal involvement was higher, accounting for 83.4%.

The standard frontline therapy for MCL is not completely unified, however, there is a general consensus that cytarabine-containing chemotherapy combined with autologous hematopoietic stem cell transplantation as the first-line treatment for young and fit patients, whereas older or unfit patients are treated with combination chemo-immunotherapy according to different tolerance(9, 20–23). Although the benefit of high-dose cytarabine is clear, due to different clinical trial results, the recognized unified regimen is not definite. In European countries, dose-intensified with cytarabine-containing regimen is recommended as induction therapy. The Nordic group (MCL2) reported the long-time follow-up results of R-maxi CHOP and R-high dose Ara-C with durable responses(24, 25). Furthermore, based on the phase 2 French study (GELA) evaluated the efficacy of R-CHOP/RDHAP, the European MCL Network confirmed the

superiority of R-CHOP/R-DHAP followed by ASCT. After a median follow-up of 6.1 years, RCHOP/ RDHAP resulted in significant improvement in TTF compared with R-CHOP followed by ASCT (109 vs. 47 months)(26, 27). On the above clinical results, the European MCL Network recommended the R-CHOP/R-DHAP as the standard induction regimen in younger MCL patients. In the USA, MD Anderson Cancer Center pioneered the regimen of R-hyper CVAD which established efficacy in younger patients and was obtained from 2 other large cohorts. Long-term follow-up showed median failure-free survival and overall survival was 6.5 years and 13.4 years in patients ≤ 65 years and the latest published MCL01 trial confirmed the efficacy of Hyper CVAD as a frontline regimen for younger patients(28–31). For young MCL patients in Asia, although experts agreement and consensus had recommended cytarabine-containing as the first-line regimen, there is no unified proposal for the concrete scheme(10). Due to treatment tolerance, patients' willingness to treatment and doctor selection, the proportion of high-dose cytarabine is still low in the real world. In our study, only 191/478 cases (39.95%) applied cytarabine-containing regimen as induction treatment in young MCL patients. Among them, 127 patients used the R-CHOP/DHAP regimen, 22 patients chose high-dose Ara C regimen, and 42 patients used dose-adjusted R-hyper CVAD regimen as induction therapy. There was no significant difference in PFS and OS between different high-dose cytarabine regimens. However, hampered by severe hematological toxicity, R-CHOP/R-DHAP is a probable better choice for Asian MCL patients in terms of therapy-associated tolerance compared with R-hyper CVAD regimen. Apart from the standard treatment options discussed above, the combined regimens containing new drugs such as BTKi or lenalidomide have been in clinical trials(32, 33). Chemotherapy-free treatment is effective in indolent lymphoma and the usage in MCL as first-line is still in the process of clinical trials(34, 3). In this cohort, 55 patients had chemo-free therapy including IR/R2/IR2 as the initial treatment. Compared with the chemo-regimen, there was no significant survival advantage, mainly because this population is elderly and unfit with the short follow-up time and lack of parallel control.

Although the role of Auto-SCT as consolidation therapy in MCL is still controversial, large-scale studies have proved that Auto-SCT can significantly improve PFS in younger, transplantation-eligible patients with MCL(15, 26, 35–37). In our study, although the proportion of Auto-SCT is low in young patients, Auto-SCT consolidation after induction was associated with significantly improved PFS and OS. Further stratification demonstrated that Auto-SCT after high-dose cytarabine as induction treatment could improve PFS, but had no significant benefit on OS, while the non-intensive treatment induction could benefit significantly in PFS and OS. The lack of improvement in OS after dose-intensified regimens may be a result of effective salvage therapy (eg, various novel agents and/or CD19-CART) after relapse, which may abrogate any improvement of consolidative Auto-CT after induction. Maintenance treatment following ASCT or induction therapy was considered standard of care for MCL patients. Based on the results of the large-scale trials, rituximab maintenance had been confirmed a significantly optimization of PFS and OS in young or eldly MCL patients(38, 39). Recently, FIL study revealed a benefit from lenalidomide maintenance after autologous transplantation with improved PFS, highlighting the role of lenalidomide maintenance in MCL(40). The role of ibrutinib in MCL maintenance treatment is in the process of clinical trials, the largest of which is the phase 3 trial Tringle study conducted by the European MCL working group. In the consensus of the Asian Lymphoma Study Group, the choice of maintenance

approach should be individualized, with cost being an important consideration(10). In our cohort, the maintenance scheme was not consistent due to affordability and reimbursement status. 44.6% patients received maintenance treatment including rituximab or lenalidomide or BTKi single or combined together, among them, 21.8% patients received rituximab maintenance therapy. Despite the majority of patients did not receive sufficient maintenance treatment time, it has been verified the efficacy of maintenance therapy in Asian patient populations. Statistics did not demonstrate the difference between different maintenance schemes, the prospective clinical trial is needed to explore the optimum maintenance scheme in the future.

The genetic instability of MCL brings about inevitable replase. Similar to previous reports, 59.0% of patients in this cohort were relapsed/refractory MCL, of which 44.6% patients were relapsed after remission. In evaluating the replased/refractory MCL, we demonstrated that elevated LDH level, initial dose-intensified therapy and maintenance treatment had significant prognostic value. Treatment choice at relapse represents a unique challenge that is dependent on various patient factors, prior therapy, remission duration. However, the past 10 years have seen a significant therapeutic advance in the treatment of MCL, novel cellular therapies and immunotherapies are currently evaluated in the relapsed/refractory setting. At present, new drugs including bortezomib, lenalidomide, ibrutinib and the new generation of BTK inhibitors zanubrutinib, obrelabrutinib, venetoclax, have been applied as single agents or in combination with immunochemotherapies or other targeted therapies in China(41–49). CD19-chimeric antigen receptor (CAR) T-cell for R/R MCL is currently being evaluated in the ongoing phase II study, and R/R MCL patients have more treatment options in China(50–52). We analyzed the remission and survival of R/R MCL patients treated with different treatment regimens in real-word. Similar to the results of MANTLE-FIRST study the report(53), patients treated with new drugs and bendamustine have improved overall survival (OS-2) than previous second-line/third-line chemotherapy, and no significant differences were observed between new drugs and bendamustine treatments. Due to the limitation of retrospective analysis, the usage of new drugs in R/R MCL patients was diverse, such as single or combination with other targeted /chemotherapy drugs, we cannot accurately evaluate the survival benefit of the single new drug. Despite the high recurrence rate, the survival of Chinese patients with mantle cell lymphoma has improved compared with previous reports.

This study is a large population-based study of MCL patients from Chinese population diagnosed over 20 years, with access to clinical data, detailed treatment, survival analysis and relapsed/ refractory selection. In summary, our study described the demographic characteristics and patient-specific data for the treatment of mantle cell lymphoma in China, demonstrated the survival benefits of initial dose-intensified therapy and auto-SCT in young Chinese patients, and further confirmed the value of maintenance treatment and explored the application of new drug treatment and bendamustine in R/R MCL patients. Although not included in this retrospective analysis, we also pay attention to the progress of molecular biology in MCL and individualized guidance, and clinical trials of new drugs in the first-line application. The treatment mode in mantle cell lymphoma may be further changed in the future.

# Declarations


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## Authors' contributions

Ping Yang, Qing-qing Cai, Wei Zhang contributed to conceptualization; Ping Yang and Shuo-zi Liu contributed to data analysis; Hong-mei Jing contributed to writing and revision; all the authors contributed to Reviewing. All authors read and approved the final manuscript.


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## Availability of data and materials

All supporting data are included in the manuscript. Additional data are available upon reasonable request to the corresponding author.

## Ethics approval and consent to participate

Informed consensus was obtained from all patients. This study was authorized by The Ethics Committee of Peking University Third Hospital.

## Consent for publication

Not applicable.

**Competing interests** The authors declare that they have no competing interests

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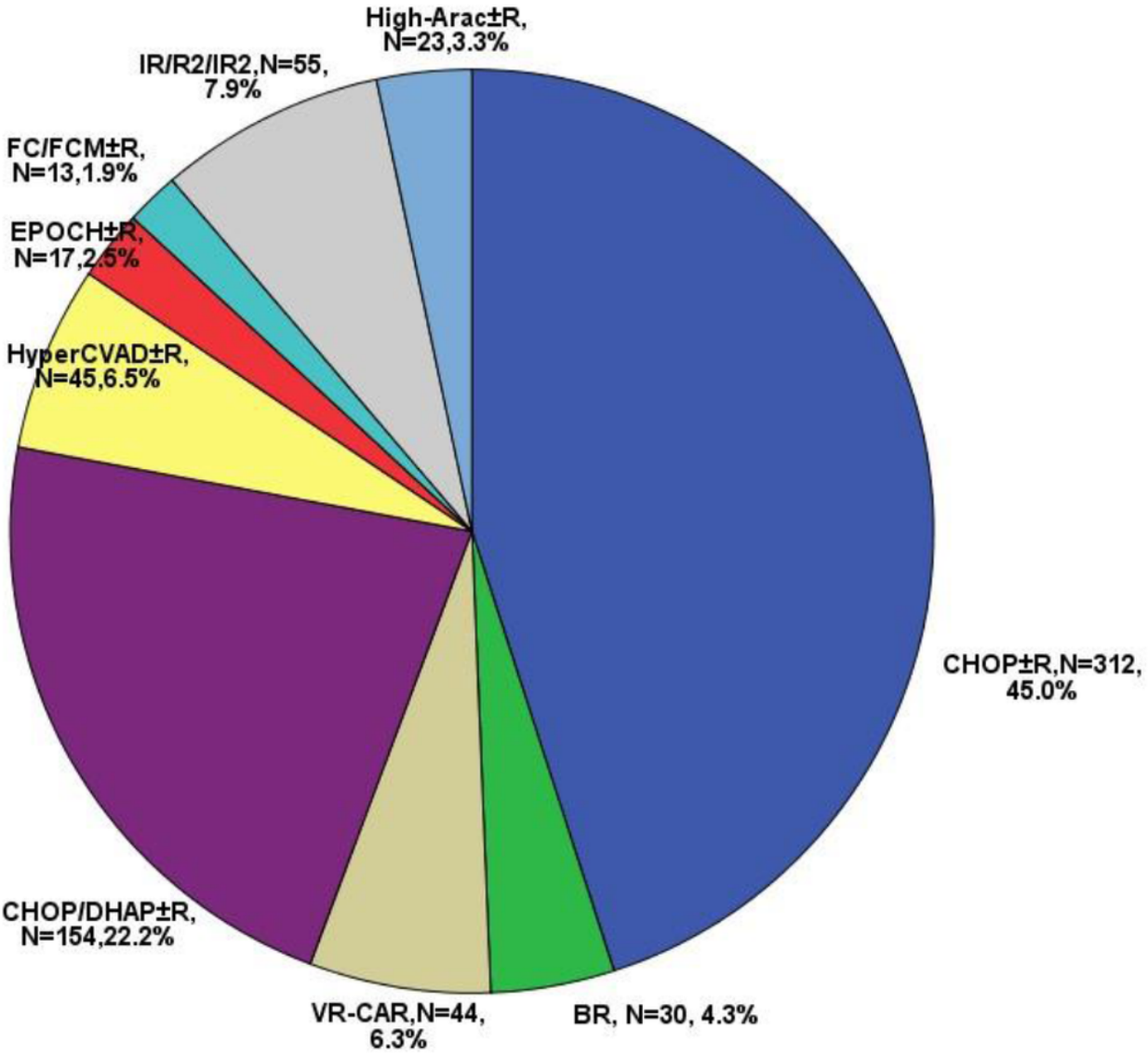
# Tables

Table 1 to 3 are available in the Supplementary Files section.

# Figures

### Figure 1

The population diagram in the study




## Figure 2

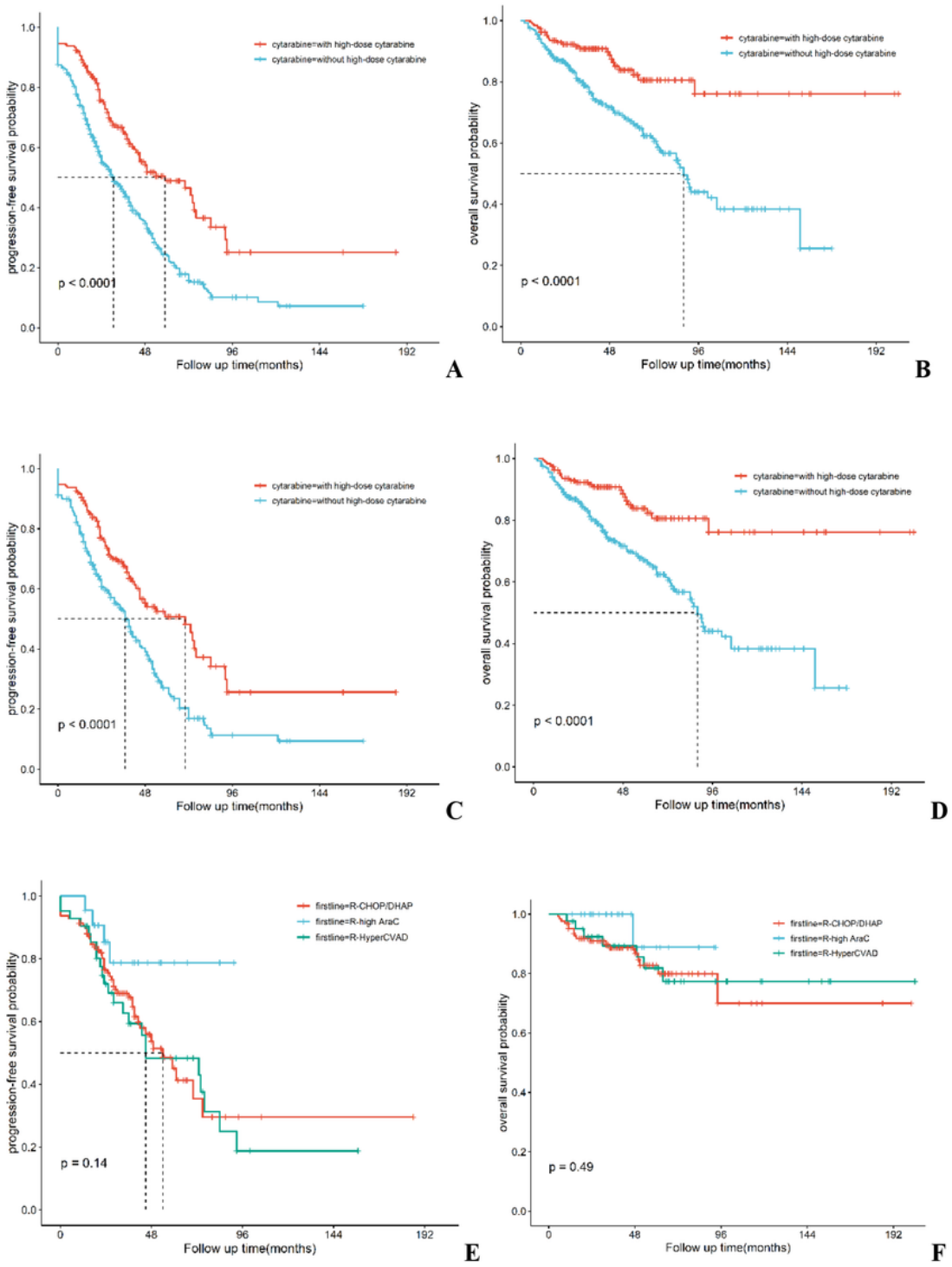
Frontline treatment choices for patients with MCL in China. CHOP±R: cyclophosphamide, doxorubicin / epirubicin, vincristineand prednisone /prednisolone plus rituximab; BR: rituximab plus bendamustine; VR-CAP: bortezomib/rituximab/cyclophosphamide/ doxorubicin/prednisolone; CHOP/ DHAP±R: cyclophosphamide, doxorubicin, vincristine and prednisone alternating with dexamethasone, high-dose cytarabine, cisplatin plus rituximab; Hyper-CVAD±R: hyperfractionated cyclophosphamide/vincristine/doxorubicin/dexamethasone; MA, methotrexate/cytarabine plus rituximab ;EPOCH±R  cyclophosphamide, epirubicin, vincristine,etoposide and prednisone plus rituximab; FC/FCM±R Fludarabine, cyclophosphamide/ Fludarabine, cyclophosphamide and mitoxantrone plus rituximab; IR/R2/IR2: Ibrutinib, rituximab/lenalidomide, rituximab/Ibrutinib, lenalidomide and rituximab High-Arac±Rhigh-dose cytarabine regimens plus rituximab except R-DHAP and Hyper-CVAD schemes.

## Figure 3

Outcomes of 693 patients with mantle cell lymphoma. (A)Progression-free survival. (B) Overall survival.

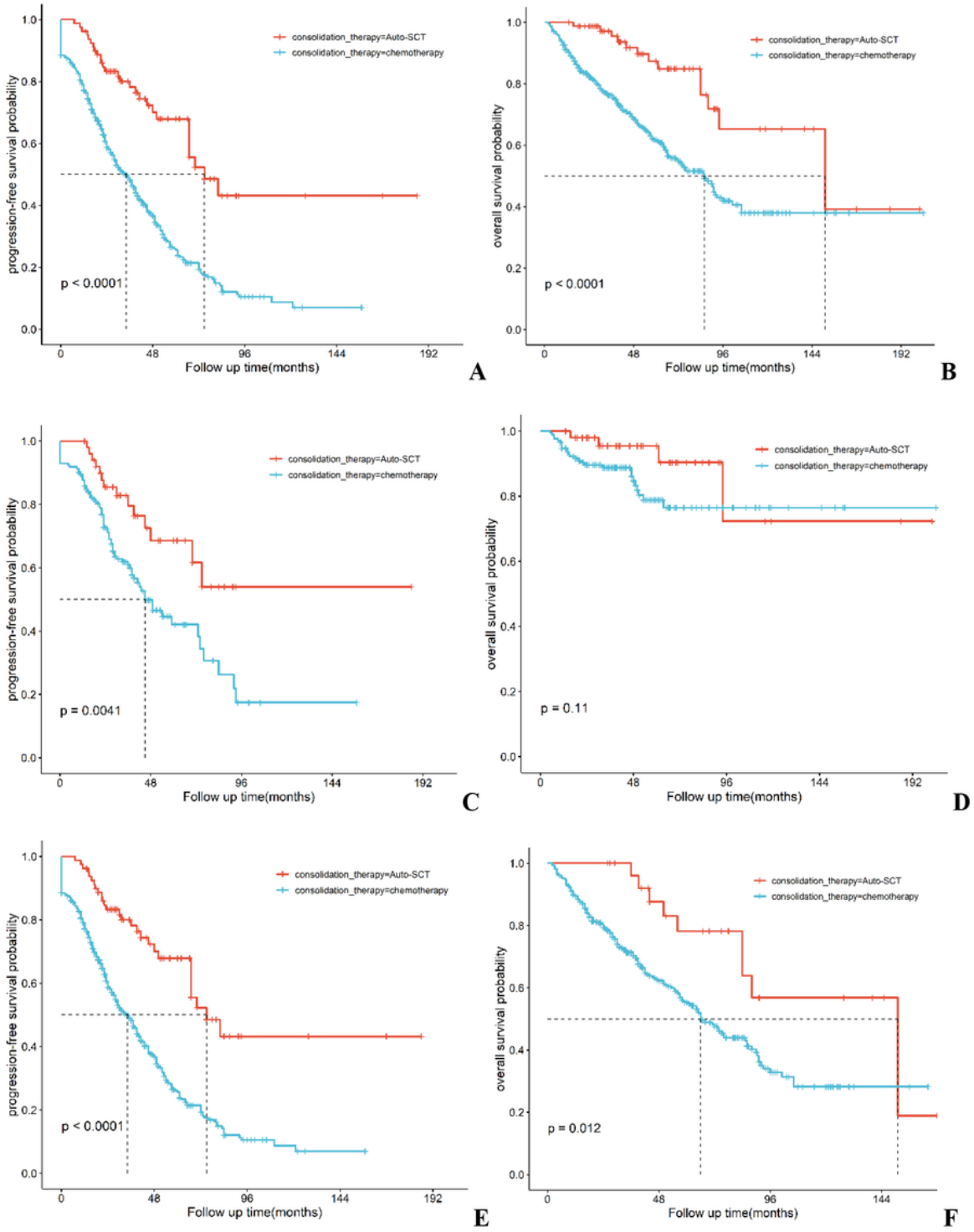
## Figure 4

Construction of the forest plots in MCL patitents. A: The independent prognostic factors in PFS according to Forest plot of Multivariate Analysis B: The independent prognostic factors in OS according to Forest plot of Multivariate Analysis.



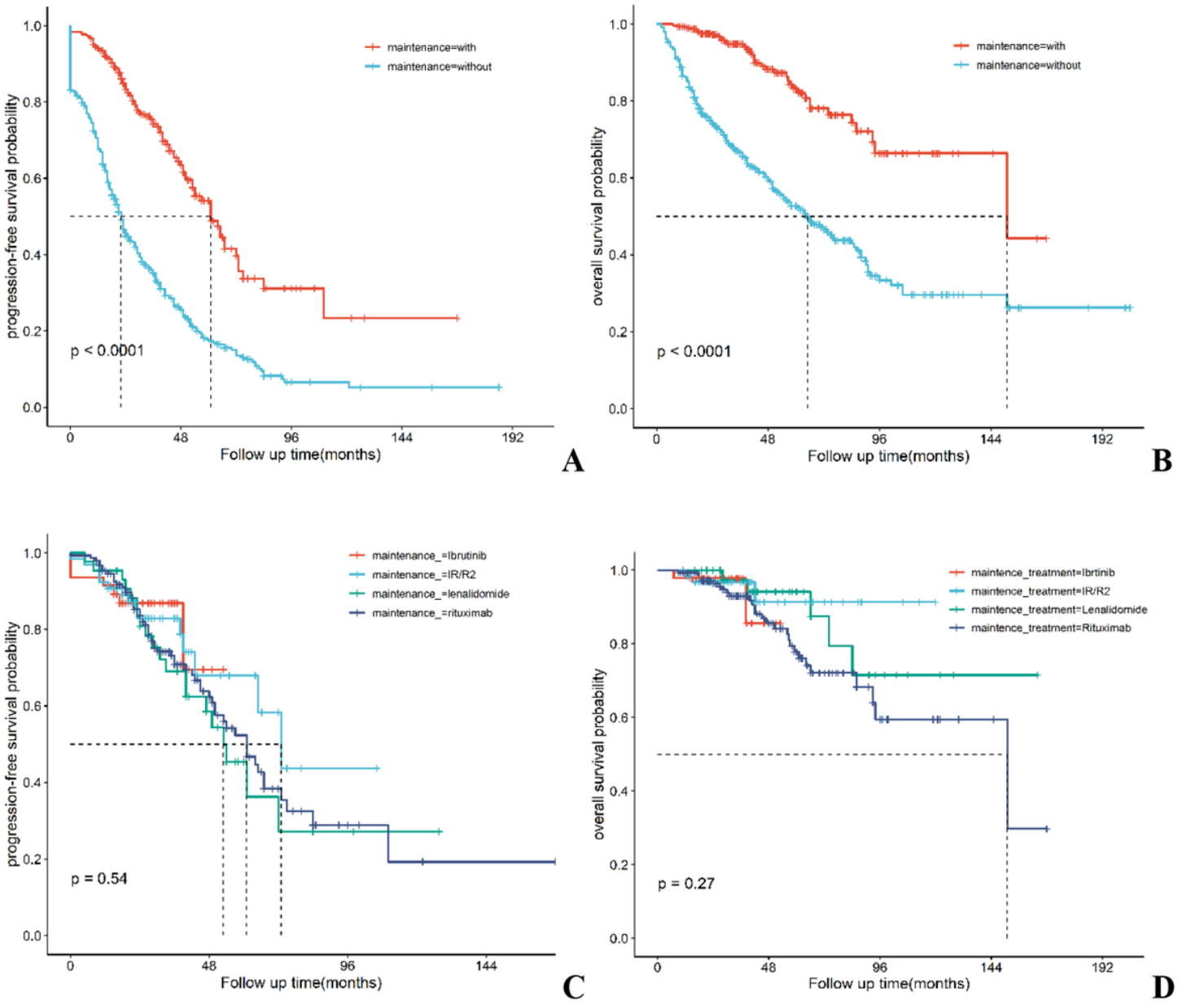

## Figure 5

Progression-free survival (A) and Overall survival (B) of patients with mantle cell lymphoma differed according to use of high-dose Arac regimens; In younger patients (age<65), use of high-dose Arac treatment showed a trend for improved PFS (C) and improved OS (D); Different high-dose cytarabine regimens show no significant difference in PFS (E) and OS(F) in younger patients.




## Figure 6

Progression-free survival (A) and Overall survival (B) of MCL patients with the usage of Auto-SCT as consolidation therapy; Induction with high-dose cytarabine, auto-SCT as consolidation therapy showed improved PFS(C) and no significant difference in OS (D) ; Induction with non-intensive chemotherapy,auto-SCT as consolidation therapy had a significant improvement in PFS(E) and OS(F).




## Figure 7

Progression-free survival (A) and Overall survival (B) of MCL patients with maintenance treatment. There is no significant difference between different maintenance therapy including rituximab, lenalidomide, ibrutinib and IR/R2 regimens in PFS (C) and OS(D).

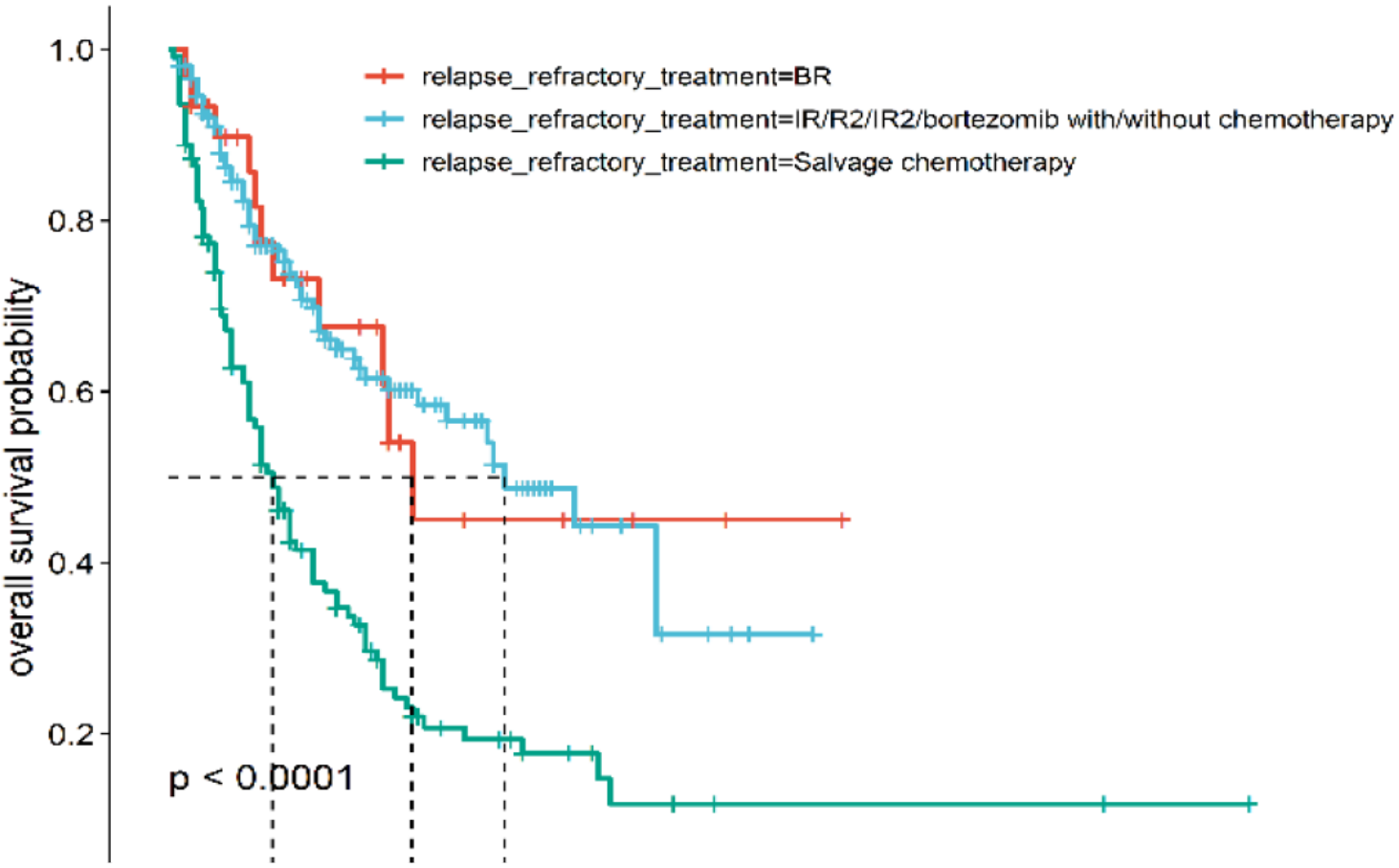



**Figure 8**

Time-to-event outcomes (OS-2) of 360 available relapsed/refractory MCL patients received treatment including salvage chemotherapy, new drug therapy and BR regimen chemotherapy.

## Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- MCLtable1.pdf
- MCLtable2.pdf
- MCLtable3.pdf.pdf