Appendix: Details of ibrutinib based regimen.

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| Trial | Regimen | Dose | Cycles |
| O’ Brien et al, 2018  (5 year f/u) (1b/2) | Ibrutinib | 420 or 840 mg PO | Continued daily until disease progression or poor tolerance |
| Burger JA et al  2014 (phase 2) | Ibrutinib  Rituximab | Ibrutinib: 420 mg PO  Rituximab: 375mg/m2 IV | Ibrutinib continued daily until progression or poor tolerance  Rituximab continued for six cycles (28 days).  Cycle 1: Every week  Cycle 2-6: Every month |
| JC Byrd et al 2014 (phase 3) | Ibrutinib | 420 mg PO daily | Continued daily until disease progression or poor tolerance |
| Farooqui et al 2014  (phase 2) | Ibrutinib | 420 mg PO daily | Continued daily until disease progression or poor tolerance |
| JA Burger et al, 2015 (phase 3) | Ibrutinib | 420 mg PO daily | Continued daily until disease progression or poor tolerance |
| Brown, J.R et al  2015 (phase 1b) | Ibrutinib  Bendamustine  Rituximab | Ibrutinib: 420 mg PO daily  Bendamustine: 70mg/m2 IV  Rituximab: 375mg/m2 (cycle 1)  500mg/m2 (cycle 2-6) | Ibrutinib continued daily until progression or poor tolerance  Bendamustine continued for 6 cycles (day 1 and 2 of each cycle)  Rituximab continued for 6 cycles (day 1 of each cycle or dose split between day and day 2) |
| Chanan-Khan et al 2016 (phase 3) | Ibrutinib  Bendamustine  Rituximab | Ibrutinib: 420 mg PO daily  Bendamustine: 70mg/m2 IV  Rituximab: 375mg/m2 (cycle 1)  500mg/m2 (cycle 2-6) | Ibrutinib continued daily until progression or poor tolerance  Bendamustine continued for 6 cycles ( cycle 1: days 2-3; cycle 2-6: days 1-2)  Rituximab continued for 6 cycles (day 1 of each cycle) |
| Susan O brien et al 2016 (phase 2) | Ibrutinib | 420 mg PO daily | Continued daily until disease progression or poor tolerance |
| JP Sharman et al 2017 (phase 3) | Ibrutinib  Ublituximab | Ibrutinib: 420 mg PO daily  Ublituximab: 900 mg IV | Ibrutinib continued daily until progression or poor tolerance  Ublituximab  Cycle 1 : day 1, day 8 , day 15  Cycle 2-6: day 1 followed by administration every third cycle |
| Burger JA et. Al 2017(Phase 2) | Ibrutinib  Rituximab | Ibrutinib: 420 mg PO daily  Rituximab: 375mg/m2 IV | Ibrutinib continued daily until progression or poor tolerance.  Rituximab continued for 6 cycles.  Cycle 1: Weekly  Cycle 2-6: Monthly |
| Jain N et al. 2017 (phase 2) | Ibrutinib  Fludarabine  Cyclophosphamide  Obinutuzumab | Ibrutinib 420 mg PO daily  Fludarabine 25mg IV  Cyclophosphamide 250 mg IV  Obinutuzumab  Cycle 1 D 1: 100mg IV  Cycle 1 D2: 900mg  Cycle 1 D8/D15: 1000 mg IV  Cycle 2/3: 1000mg IV | Ibrutinib continued daily for a maximum of 12 cycles.  Fludarabine continued for 3 cycles.  Cycle 1: Day 2-4  Cycle 2-3: Day 1-3  Cyclophosphamide continued for 3 cycles  Cycle 1: Day 2-4  Cycle 2-3: Day 1-3  Obinutuzumab continued for a maximum of 6 cycles  Cycle 1 : D1, D2, D8, D15  Cycle 2-6: D1 |
| Davids MS.et 2017 (phase 2) | Ibrutinib  Fludarabine  Cyclophosphamide  Rituximab | Ibrutinib 420 mg PO daily.  Fludarabine at standard dosing  Cyclophosphamide at standard dosing  Rituximab at standard dosing | Ibrutinib started 7 days prior to FCR and continued until progression or poor tolerance  Fludarabine continued for 6 cycles  Cyclophosphamide continued for 6 cycles  Rituximab continued for 6 cycles |
| Rogers KA HYet al 2017 (phase 1b2) | Ibrutinib  Obinutuzumab  Venetoclax | - | - |