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 toleranceRituximab continued for six cycles (28 days).Cycle 1: Every weekCycle 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 al2015 (phase 1b) | IbrutinibBendamustineRituximab | Ibrutinib: 420 mg PO dailyBendamustine: 70mg/m2 IVRituximab: 375mg/m2 (cycle 1)500mg/m2 (cycle 2-6) | Ibrutinib continued daily until progression or poor toleranceBendamustine 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) | IbrutinibBendamustineRituximab | Ibrutinib: 420 mg PO dailyBendamustine: 70mg/m2 IVRituximab: 375mg/m2 (cycle 1)500mg/m2 (cycle 2-6) | Ibrutinib continued daily until progression or poor toleranceBendamustine 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) | IbrutinibUblituximab | Ibrutinib: 420 mg PO dailyUblituximab: 900 mg IV  | Ibrutinib continued daily until progression or poor toleranceUblituximabCycle 1 : day 1, day 8 , day 15Cycle 2-6: day 1 followed by administration every third cycle |
| Burger JA et. Al 2017(Phase 2) | IbrutinibRituximab | Ibrutinib: 420 mg PO dailyRituximab: 375mg/m2 IV | Ibrutinib continued daily until progression or poor tolerance.Rituximab continued for 6 cycles.Cycle 1: WeeklyCycle 2-6: Monthly  |
| Jain N et al. 2017 (phase 2) | Ibrutinib FludarabineCyclophosphamideObinutuzumab | Ibrutinib 420 mg PO dailyFludarabine 25mg IV Cyclophosphamide 250 mg IVObinutuzumabCycle 1 D 1: 100mg IVCycle 1 D2: 900mgCycle 1 D8/D15: 1000 mg IVCycle 2/3: 1000mg IV | Ibrutinib continued daily for a maximum of 12 cycles.Fludarabine continued for 3 cycles.Cycle 1: Day 2-4Cycle 2-3: Day 1-3Cyclophosphamide continued for 3 cyclesCycle 1: Day 2-4Cycle 2-3: Day 1-3Obinutuzumab continued for a maximum of 6 cyclesCycle 1 : D1, D2, D8, D15Cycle 2-6: D1 |
| Davids MS.et 2017 (phase 2) | IbrutinibFludarabineCyclophosphamideRituximab | Ibrutinib 420 mg PO daily.Fludarabine at standard dosingCyclophosphamide at standard dosing Rituximab at standard dosing | Ibrutinib started 7 days prior to FCR and continued until progression or poor toleranceFludarabine continued for 6 cyclesCyclophosphamide continued for 6 cyclesRituximab continued for 6 cycles |
| Rogers KA HYet al 2017 (phase 1b2) | IbrutinibObinutuzumabVenetoclax | - | - |