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SOUTHAMPTON LYMPHOMA GROUP TRIALS PORTFOLIO (October 2024)

Study Title	Treatment	Phase	Key inclusion criteria	Key exclusion criteria
DLBCL First line				
REMoDL-A (CAN1500)	RCHOP vs acalabrutinib-RCHOP	Phase II	≥16 years -Fit for a full course of chemo	-Previous treated/untreated indolent lymphoma unless newly diagnosed discordant lymphoma.
STELLAR (CAN1495)	CHOP-R in combination with acalabrutinib compared to CHOP-R in patients with newly diagnosed Richter's Syndrome (RS)	Phase II	≥16 years -Suitable for anthracycline-containing chemo-immunotherapy. -Patients with CLL and newly diagnosed biopsy proven DLBCL-type RS.	-Any prior treatment with CHOP/ Anthracycline therapy -Prior ibrutinib exposure within 4 weeks of RS diagnosis -prior acalabrutinib exposure
ZUMA-23 (CAN1729)	Randomised • Axicabtagene ciloleucel • SOC	Phase III	≥18 years -newly diagnosed high risk LBCL [IPI≥4]	-Any prior treatment (other than 1 cycle of RCHOP prior to randomization) -PCNSL, TCR-LBCL, PMBCL, LBCL (unclassifiable), Burkitt
EPCORE (CAN1703) **Recruitment Pause**	Epcoritamab (CD20/CD3 bispecific) +/- lenalidomide	Phase II	- Stage II-IV newly diagnosed de novo DLBCL or transformed from FL, nMZL, FL-g3b -Ineligible for anthracycline-based therapy/cytotoxic chemo due to: ○ Being age ≥80 years; AND/OR ○ Being age ≥75 years and having important comorbid condition(s)	-Known active, clinically significant infection -Severe cardiovascular disease (other than those eligibility criteria that preclude the subject from receiving anthracycline-based therapy/cytotoxic chemo)

DLBCL Relapsed/Refractory				
POLA-R-ICE (CAN1639)	Polatuzumab vedotin plus rituximab, ifosfamide, carboplatin and etoposide (Pola-R-ICE) with R-ICE alone as salvage therapy in patients with primary refractory or relapsed diffuse large B-cell lymphoma (DLBCL)	Phase III	≥16 years -primary refractory or relapsed aggressive B-NHL -On first relapse	-CNS lymphoma -Richter's transformation or prior CLL -Received >1 line of therapy for DLBCL -Received polatuzumab vedotin as part of first line therapy
NURIX (CAN1655)	NX-5948, a Bruton's Tyrosine Kinase (BTK) Degrader, in Adults with Relapsed/ Refractory B-cell Malignancies	Phase I	≥18 years -histologically confirmed R/R CLL, SLL, DLBCL, FL, MCL, MZL, or WM. -Received at least 2 prior systemic therapies, (or at least 1 prior therapy for WM)	-strong or moderate cytochrome P450 3A (CYP3A) inhibitors or inducers within 14 days or 5 half-lives -Prior ASCT or CAR-T within 100days -Prior small molecule therapy within 4 weeks or 5 half-lives
DTP3 (CAN1700)	Dose escalation and dose expansion DTP3 administered as a one-hour infusion three times per week	Phase I/II	>16 years -Not currently a candidate for stem cell transplant or CAR T-cell therapy	-Stem cell or CAR T-cell within 12 weeks of consent, or other IMP within 28 days. -Prior non-experimental therapy or radiotherapy within 28 days.
ATHENA-1 (CAN1607)	REGN5837 + Odronextamab in aggressive B-Cell NHLs	Phase I	≥18 years -CD20+ aggressive B-NHL - progression after at least 2 lines of systemic therapy containing an anti-CD20 antibody and an alkylating agent -Patients who have received CAR-T therapy are eligible	-Prior allogeneic stem cell transplantation or solid organ transplantation -Prior treatment with anti-CD20 x anti-CD3 bispecific antibody, such as odronextamab
CC-99282-NHL-001 (CAN1672) **Recruitment WL**	CC-99282 (small molecule cereblon E3 ligase modulator) alone vs Valemetostat+Rituximab Cohort G Safety Run-in	Phase I	≥18 years -- R/R DLBCL, FL 3b -Received at least 2 lines of therapy, or have received 1 line and are not eligible for ASCT	- < 4 weeks from prior CAR-T, T-cell engaging drugs, CRBN-modulators; <3 months from autoPBSCT, <6 months from alloBMT - Strong CYP3A4/5 inhibitors

OLYMPIA-6 (CAN1838) *In set up*	*Randomised* *Post 2nd line CAR T* • *REGN1979* • *Observation*	*Phase III*	*≥18 years* *-CAR T at least 28 days before* *-ECOG≤1* *-recovery from CAR T to G1 or baseline*	*-P or S CNSL* *-history or current CNS pathology* *-No other anti-lymphoma between CAR T and study*
PORTAL (CAN1816) *Awaiting set up*	*Single Arm* *Pola-Glofib 2 cohorts, as bridging to CAR T after 2 cycles or up to 12 cycles*	*Phase II*	*≥18 years* *DLBCL, HGBCL with myc, bcl2 and/or bcl6, HGBCL NOS, PMBCL, Transformed FL* *-Part 1 -R/R eligible for CAR T and need bridging. ECOG 0/1* *-Part 2 Failed to achieve CMR D score 1-3, ECOG 0-2*	*≥G2 peripheral neuropathy* *CNS Lymphoma* *Active AI or Immunodeficiency* *Concomitant severe neuro disorder* *Prior soldi organ transplant* *Prior allo SCT* *Auto SCT within 100 days* *Known or suspected HLH* *(prior Pola is not an exclusion)*
Primary CNS Lymphoma				
OptiMATE (CAN1699)	De-escalated induction tx in PCNSL - randomised • Arm A/ control - 4 cycles of MATRix • Arm B/ experimental - R/HD-MTX followed by 2 cycles of Matrix	Phase III	-Newly diagnosed -Disease exclusively located in the CNS -Previously untreated (steroids permitted)	-Congenital or acquired immunodeficiency inc HIV and previous organ transplantation
FL First line				
PETREA (CAN1368)	Evaluation of utility of FDG PET: Induction (BR vs RCHOP vs RCVP- investigator's choice) then R vs no R maintenance (if PET neg) or R-len (PET pos)	Phase III	≥18 years -documented diagnosis of follicular lymphoma (grade 1, 2 or 3a). -non-contiguous stage II, stage III, or stage IV. -Must fulfil at least one of the GELF criteria for high tumour burden	-CNS involvement
CAN1848 *In set up*	*IV AZD0486 (D19xCD3 bispecific TCE) +RCHOP* *Previously untreated FL3B*	*Phase I,II*	*Untreated FL3B*	*-Leukaemic presentation*

CA073-1022 CAN1847 *Awaiting set up*	*Randomised Golcadomide + Rituximab in newly dxed advanced stage FL*	*Phase II*	*TBC*	*TBC*
FL Relapsed/Refractory				
NURIX (CAN1655)	NX-5948, a Bruton's Tyrosine Kinase (BTK) Degrader, in Adults with Relapsed/Refractory B-cell Malignancies	Phase I	≥18 years -histologically confirmed R/R CLL, SLL, DLBCL, FL, MCL, MZL, or WM. -Received at least 2 prior systemic therapies, (or at least 1 prior therapy for WM)	-Strong or moderate cytochrome P450 3A (CYP3A) inhibitors or inducers within 14 days or 5 half-lives -Prior ASCT or CAR-T within 100 days -Prior small molecule therapy within 4 weeks or 5 half-lives
ZUMA-22 (CAN1709)	Randomised • Axicabtagene Ciloleucel • SoC	Phase III	≥ 18 years -1 prior line of systemic chemoimmunotherapy with high-risk disease or after ≥ 2 prior lines of systemic therapy	-Known history or suspicion of CNS lymphoma involvement -History of large B cell lymphoma or transformed FL -FL grade 3b -Small lymphocytic lymphoma -Lymphoplasmacytic lymphoma
Mahogany BGB-3111-308 (CAN1747)	Randomised 1:1 • Zanubrutinib+Obinutuzumab • Rituximab+Lenalidomide,R^2	Phase III	≥ 18 years -G1-3a FL -previous at least 1 line systemic, antiCD20 -ECOG 0-2	-transformation to aggressive L -prior BTKi -prior Lenalidomide -neuropathy G>1
ATHENA-1 (CAN1607)	REGN5837 + Odronextamab in aggressive B-Cell NHLs	Phase I	≥18 years -CD20+ aggressive B-NHL - progression after at least 2 lines of systemic therapy containing an anti-CD20 antibody and an alkylating agent -Patients who have received CAR-T therapy are eligible	-Prior allogeneic stem cell transplantation or solid organ transplantation -Prior treatment with anti-CD20 x anti-CD3 bispecific antibody, such as odronextamab

CC-99282-NHL-001 (CAN1672) **Recruitment WL**	CC-99282 (small molecule cereblon E3 ligase modulator) alone vs Valemetostat H Safety Run-in CC-99282 alone vs in combination with rituximab Cohort D	Phase I	≥18 years -- R/R FL 1-3a -Received at least 2 lines of therapy, or have received 1 line and are not eligible for ASCT -Cohort D -received at least 1 lines of therapy	- < 4 weeks from prior CAR-T, T-cell engaging drugs, CRBN-modulators; <3 months from autoPBSCT, <6 months from alloBMT - Strong CYP3A4/5 inhibitors
Mantle Cell Lymphoma First line				
ZEBRA (CAN 1798) *In set up*	*Randomised* • *Zanubrutinib+Rituximab fixed duration* • *Observation*	*Phase II*	*≥18 years* *-Pathologically confirmed MCL with t(11;14) and/or overexpress cyclin D1,D2 or D3* *-Stage II-IV by CT or by WCC/BM infiltration* *- Indolent MCL* ○ *Observation without treatment for minimum 6 months* ○ *Leukaemic non-nodal variant* ○ *Low tumour volume (LN ≤ 3cm, Ki67 ≤ 30% and classical morphology – non-blastoid/pleomorphic*	*-any prior treatment for MCL including RT* *-CNS involvement* *-no progression requiring treatment since diagnosis* *-moderate or strong CYP3A inducer* *- vitamin K antagonist* *- active or history of bleeding or history of spontaneous bleeding requiring blood transfusion or other medical intervention* *- history of stroke or ICH within 6 months*
Mantle Cell Lymphoma Relapsed/Refractory				
NURIX (CAN1655)	NX-5948, a Bruton's Tyrosine Kinase (BTK) Degrader, in Adults with Relapsed/ Refractory B-cell Malignancies	Phase I	≥18 years -histologically confirmed R/R CLL, SLL, DLBCL, FL, MCL, MZL, or WM. -Received at least 2 prior systemic therapies, (or at least 1 prior therapy for WM)	-strong or moderate cytochrome P450 3A (CYP3A) inhibitors or inducers within 14 days or 5 half-lives -Prior ASCT or CAR-T within 100days -Prior small molecule therapy within 4 weeks or 5 half-lives
Other B-NHL				

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DTP3 (CAN1700)	Dose escalation and dose expansion DTP3 administered as a one-hour infusion three times per week	Phase I/II	>16 years -Not currently a candidate for stem cell transplant or CAR T-cell therapy	-Stem cell or CAR T-cell within 12 weeks of consent, or other IMP within 28 days. -Prior non-experimental therapy or radiotherapy within 28 days.
CAN1848 *In set up*	*IV AZD0486 (D19xCD3 bispecific TCE) +RCHOP*		*-R/R B NHL post 1st line* *-presence of CD19 expression in previous CD19-directed therapy*	*-Current diagnosis of* ○ *BCL unclassifiable, features bet DLBCL and classical HL (mediastinal grey-zone L)* ○ *Burkitt Lymphoma* ○ *Richter's transformation* ○ *Primary effusion DLBCL* ○ *P or S CNS L* *-Leukaemic presentation*
Hodgkin Lymphoma FL				
RADAR (CAN1666) *In set up*	*Randomised* *PET response adapted design* *Untreated Stage IA/IIA HL* • *ABVD+/-ISRT* • *A2VD+/-ISRT*	*Phase III*	*16-69 years* *Stage IA/IIA with no mediastinal bulk*	*- Previous treatment for HL apart from short courses of oral steroid* *-infradiaphragmatic disease* *-NLPHL* *-other active cancer with exceptions* *-grade ≥1 sensory or motor peripheral neuropathy from any cause*
RATiFY (CAN1835) *Awaiting set up*	*Non-randomised* *Initial x 3 tislelizumab > iPET+ceCT > Group A-E*	*Phase II*	*≥60 years* *-ECOG 0-2* *-EF≥50%* *-CrCL≥30ml/min*	*-NLPHL* *-History of AI within 2 years* *-Solid organ transplant* *-≥G2 peripheral neuropathy*

	• *GpA – RT+ x 2 years of Tislelizumab* • *GpB to E – tislelizumab+AVD (2-6 cycles)+/-RT*			*-presented with symptomatic compression of vital structures* *-Immunosuppressive therapy within 2 months* *-treated haematological malignancy* *-solid organ malignancy in last 3 yrs*
Hodgkin Lymphoma Relapsed/Refractory				
PTCL				
CCS1477 (CAN1483)	CCS1477 (oral bromodomain inhibitor of p300/CBP) monotherapy in advanced haem malignancies	Phase I/IIa	≥2 previous lines of therapy Specific Molecular sub-group (to contact Southampton trials team)	-Strong CYP3A4 inducers or inhibitors within 4 weeks of first dose
BI-1808 (CAN1605)	TNFR2 mAb monotherapy and in combination with pembrolizumab (currently in phase 1)	Phase I/IIa	-Any histologically confirmed advanced malignancy -Has received SOC or ineligible for SOC	-Active CNS metastases -Systemic treatment within 4 weeks of first dose -Radiotherapy within 2 weeks of first dose of BI-1808.
CLL				
NURIX (CAN1655)	NX-5948, a Bruton's Tyrosine Kinase (BTK) Degrader, in Adults with Relapsed/Refractory B-cell Malignancies	Phase I	≥18 years -histologically confirmed R/R CLL, SLL, DLBCL, FL, MCL, MZL, or WM. -Received at least 2 prior systemic therapies, (or at least 1 prior therapy for WM)	-strong or moderate cytochrome P450 3A (CYP3A) inhibitors or inducers within 14 days or 5 half-lives -Prior ASCT or CAR-T within 100days -Prior small molecule therapy within 4 weeks or 5 half-lives
CELESTIAL CAN1789 *In set up*	*Randomised 1:1* • *BGB-11417 Sonrotoclax+ Zanubrutinib vs* • *Venetoclax+ Obinutuzumab in Untreated CLL/SLL*	*Phase III*	*≥18 years* *-ECOG 0-2* *-CLL requiring treatment*	*-previous systemic treatment (up to x4 doses of anti CD20 for AI cytopenia is allowed)* *-PLL or Richter's* *-CNS involvement* *-Significant cardiovascular disease*