Early Clinical Trials

Implementing a phase I/II Clinical Trial Unit (Early Clinical Trial Unit, ECTU) in September 2012 started with the acquirement of GMP by the clinical pharmacy, identification and realization of a new central location for this CCCF-ECTU on the UKF campus, increase of the activities within the DKTK and establishment of preferred partnerships. All these were prerequisites for the improvement of the conduct of early clinical trials within the CCCF and UKF.

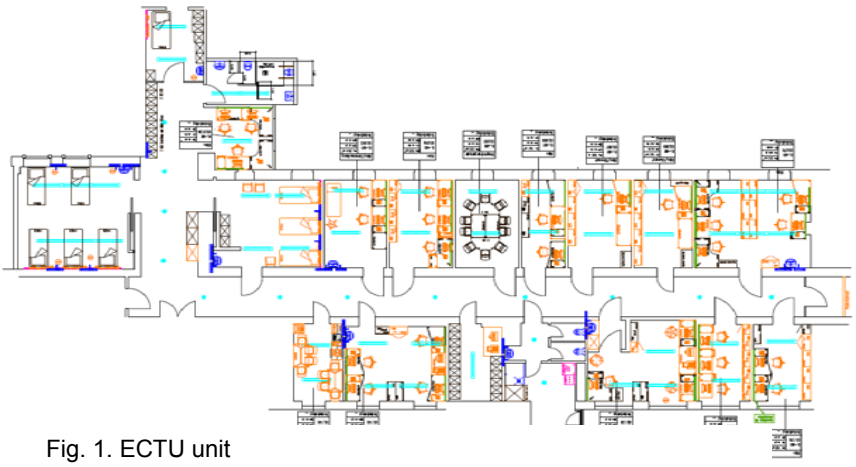


Fig. 1. ECTU unit

In 2012/2013, realization of a new central location for the ECTU was achieved with valuable UKF and CCCF support and eager encouragement of the clinical (J.Duyster), scientific (C.Peters) and executive (R.Bredenkamp) CCCF directors as well as UKF departments, one major CCCF target being to put more emphasis on the conduct of early clinical trials. Implementation of this new CCCF ECTU swiftly succeeded within 3 months of reconstruction and renovation, whereby a spacious ECTU with 6 beds (3 for outpatient care and 3 for inpatients) was completed in the facilities of the former emergency unit of the medical department in January 2013 (Fig. 1). Study nurse support, study coordination, monitoring, chemotherapy-management, pharmacology, tumor-base-documentation were all integrated within this new unit and all necessary medical equipment (monitors, infusion pumps, ECG, emergency equipment) was employed therein. Moreover, all trial-specific equipment is in place within this ECTU (centrifuges, refrigerators, study medication storage room, monitoring and study audit capacities), thus realizing an efficacious and well-organized in- and outpatient facility for the entire CCCF. Another major advantage of this ECTU is, that it is adjacent to the leukemia ward (24-hour physician and nursing support) and both intensive care units are also located in the medical department building. This central location and easy access to intensive care units and other UKF departments makes this ECTU a well frequented and busy study facility.

Increasing numbers of early clinical trials have been drawn to this newly established ECTU since 1/2013: of note, of initially 7 phase I studies in 2013 (2 in hematology/oncology), phase I trial numbers have substantially increased to 21 in 2015 (14 currently enrolling [Fig. 2] and 7 being in preparation to start within this ECTU shortly). Tumor entity-specific early clinical trials involve both solid tumor and hematologic malignancies as shown from the ECTU start in 1/2013 through 2015 (Fig. 2).

Current ECTU trials involve innovative target drugs both for hematological and solid tumor patients as examplified in Table1.

Fig. 2. Phase I clinical trials from ECTU start 1/2013 -> 2015

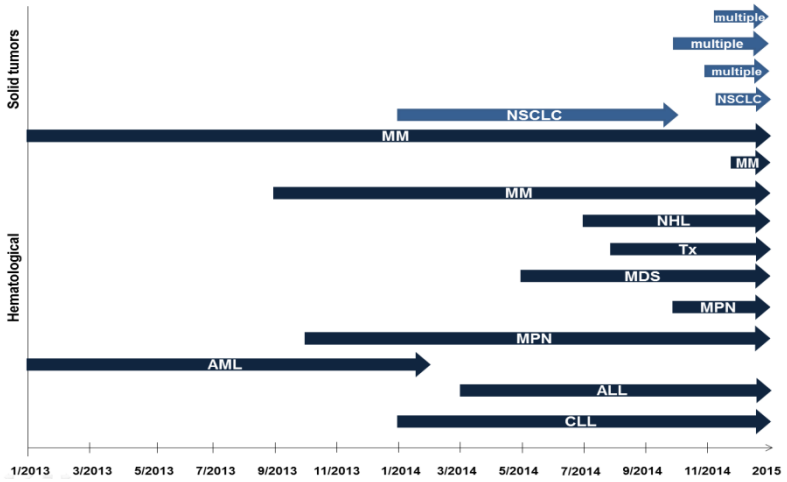


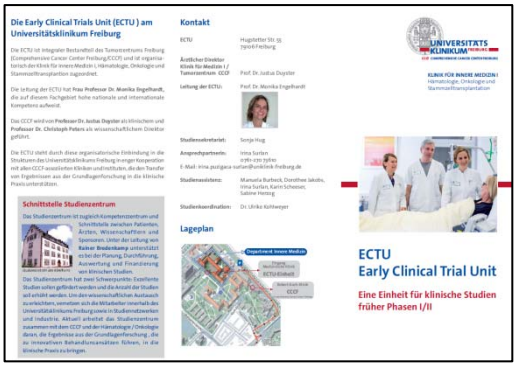
Table 1. Selected ECTU trials 2015

α PD-L1 Ab (MSB0010718C)	Solid tumors (Gastric, Melanoma, Ovarian, ACC, Mesothelioma, Urothelial)
α PD-L1 Ab (MPDL3280A)	mCRC (kras+), NSCLC, Melanoma (kras+)
c-MET inhibitor (INC280)	c-MET dependent advanced solid tumors
c-MET inhibitor (INC280)	NSCLC (EGFR+)
VBDD (Vorinostat, HDAC inhibitor)	RR multiple myeloma
α CD38 Ab (MOR03087)	RR multiple myeloma
Proteasome inhibitor (Carfilzomib)	RR multiple myeloma
α CD20 biosimilar (BI 695500)	NHL
KRP203	Allo-Tx
PLK-1 inhibitor (Volasertib)	Untreated MDS
HDAC inhibitor (Givinostat)	Jak2 positive PV (MPN)
Ruxolitinib + Pomalidomid	MPN
Treosulfan-Fludarabin-Thiotepa Kond.	ALL, 2nd allo-Tx
BCL-2 inhibitor (GDC-0199/ ABT-199)	RR CLL

Important incitement and support for this ECTU comes from J.Duyster (director Department of Hematology/Oncology, clinical CCCF director), M.Engelhardt (medical lead ECTU), and R.Bredenkamp (director Clinical trial center, ECTU lead, executive director CCCF) promoting this CCCF unit in any respect. To support this ECTU both clinically and scientifically, two additional attending physicians were recruited therein (L.Illert, A. Krohn).

Essential departmental collaborations with CCCF departments have been successfully intensified in terms of ECTU activities, such as with the gynecology (E.Stickeler) or gastroenterology (R. Thimme) that perform their early clinical trials also within this ECTU facility. Relevant external preferred partnerships have been established, e.g. with the CRO Quintiles and industry: with Novartis, the ECTU is now 'preferred partner' for phase I/II trials and OTM center. Others are in preparation to follow, such as Roche and CRO Parexcel.

Fig. 3. Promotion ECTU flyer



Promotions and public relation incentives have eagerly been performed with implementation of an ECTU flyer, ECTU-homepage and promotion articles (e.g. within CCCF and UKF magazines; Fig. 3). Various ECTU presentations within the UKF and external visits and meetings have been realized by M.Engelhardt, R.Bredenkamp, J.Duyster and ECTU-principle investigators.

Moreover, a patient feed-back questionnaire on the ECTU (Fig. 4) and its performance was developed and patient responses are regularly analyzed. Patient responses on the ECTU have been exceptionally good: organization, study nurse, nursing and physician support, information provision on novel agents and the respective phase I studies was judged as excellently performed and the unit premises and hygiene are highly appraised.

Fig. 4. ECTU patient feed-back questionnaire

Due to the success story of the ECTU, this important phase I unit will also move to the interdisciplinary cancer center (ITZ; Fig. 5) building that is planned for 2017/18 and will explicitly continue to promote both clinical trials and CCCF activities in any respect.

The ECTU has been inspected by the regional authority Baden-Württemberg and passed masterfully both KTQ-certification and OnkoZert visits 3/2014 and 11/2014, respectively.

Fig. 5. New ITZ building, where ECTU will be integrated for CCCF benefits and easy access purposes in 2017/18