to RNA-sequencing and high-resolution mass spectrometry to identify RNA, metabolite, and lipid profiles. Differentially expressed transcripts, metabolites, and lipids were identified and their biological significance assessed by pathway analysis. Multivariate analysis method DIABLO (R package mixOmics) was used to integrate the molecular changes characterizing the CSF of MB patients. Differentially expressed transcripts, metabolites, and lipids in CSF were discriminatory for the presence of MB but not the exact molecular subtype. One hundred ten genes and ten circular RNAs were differentially expressed in MB CSF compared to normal representing TGF-β signaling, TNF-a signaling via NF-kB, and adipogenesis pathways. Tricarboxylic acid cycle and other metabolites (malate, fumarate, succinate, α-ketoglutarate, hydroxypyruvate, N-acetyl-aspartate) and total triacylglycerols were significantly upregulated in MB CSF compared to normal CSF. Although the transcriptomic, metabolomic, and lipid signatures in CSF to differentiate MB subgroup separation was challenging, we were able to identify a group of omics signatures that could separate cancer from normal CSF. Metabolic and lipidomic profiles both contained indicators of tumor hypoxia. Our approach provides several candidate signatures that deserve further validation, including the novel circular RNA circ_463, and insights into the impact of MB on the CSF microenvironment.

MEDB-04. YOUNG CHILDREN WITH METASTATIC MEDULLOBLASTOMA: FREQUENT REQUIREMENT FOR RADIOTHERAPY IN CHILDREN WITH NON-WNT/NON-SHH MEDULLOBLASTOMA DESPITE HIGHLY INTENSIFIED CHEMOTHERAPY – RESULTS OF THE MET-HIT2000-BIS4 TRIAL

Martin Mynarek[1,2], Tobias Goschzik[3], Marcel Kool[4,5], Katja von Hoff[6], Holger Ottensmeier[7], Monika Warmuth-Metz[8], Brigitte Bison[9], Martin Sill[10,11], Elisabeth Jane Rushing[12], Martin Hasselblatt[13], Arend Koch[14], Ulrich Schüller[15,16], Andreas von Deimling[17,18], Markus J. Riemenschneider[19], Hildegard Dohmen[20], Camelia-Maria Monoranu[21,22], Clemens Sommer[23], Ori Staszewski[24,25], Christian Mawrin[26], Jens Schittenhelm[27], Wolfgang Brück[28], Katharina Filipski[29,30], Christian Hartmann[31], Matthias Meinhardt[32], Klaus Pietschmann[33], Christine Haberler[34], Irene Slavc[35], Nicolas U. Gerber[36,37], Michael Grotzer[36,37], Martin Benesch[38], Paul-Gerhardt Schlegel[39], Frank Deinlein[40], Udo Bode[41], André O. von Bueren[42,43], Carsten Friedrich[44], Denise Obrecht[15], Gudrun Fleischhack[45], Robert Kwiecien[46], Andreas Faldum[46], Rolf-Dieter Kortmann[47], Torsten Pietsch[48], Stefan Pfister[4,49], Stefan Rutkowski[15]; [1]Pediatric Hematology and Oncology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany. [2]Mildred Scheel Cancer Career Center HaTriCS [4], University Medical Center Hamburg-Eppendorf,, Hamburg, Germany. [3]nstitute of Neuropathology, Brain Tumor Reference Center of the German Society for Neuropathology and Neuroanatomy (DGNN), Bonn, Germany. [4]Hopp Children's Cancer Center at the NCT Heidelberg (KiTZ) and Division of Pediatric Neurooncology (B [062]), German Cancer Research Center (DKFZ) and German Cancer Consortium (DKTK), Heidelberg, Germany. [5]Princess Máxima Center for pediatric oncology, Utrecht, Netherlands. [6]Department of Pediatric Oncology, Charite – Universitätsmedizin Berlin, Berlin, Germany. [7]epartment of Pediatric Hematology and Oncology, University Children's Hospital Wuerzburg, Würzburg, Germany. [8]Institute of Diagnostic and Interventional Neuroradiology, University Hospital Wuerzburg, Würzburg, Germany. [9]Department of Neuroradiology, University Hospital Augsburg, Augsburg, Germany. [10]Hopp Children's Cancer Center at the NCT Heidelberg (KiTZ), Heidelberg, Germany. [11]Division of Pediatric Neurooncology (B[062]), German Cancer Research Center (DKFZ) and German Cancer Consortium (DKTK), Heidelberg, Germany. [12]Institute of Neuropathology, University Medical Center Zurich, Zurich, Switzerland. [13]Institute of Neuropathology, University Hospital Muenster, Münster, Germany. [14]Department of Neuropathology, Charite – University Medical Center Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität Berlin, and Berlin Institute of Health, Berlin, Germany. [15]Department of Pediatric Hematology and Oncology, University Medical Center Hamburg Eppendorf, Hamburg, Germany. [16]Department of Neuropathology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany. [17]Clinical Cooperation Unit Neuropathology (B [300]), German Cancer Research Center (DKFZ), Heidelberg, Germany. [18]Department of Neuropathology, Heidelberg University Hospital, Heidelberg, Germany. [19]Department of Neuropathology, Regensburg University Hospital, Regensburg, Germany. [20]Institute for Neuropathology, University Hospital Gießen and Marburg, Gießen, Germany. [21]Institute of Pathology, Department of Neuropathology, University of Wuerzburg, Würzburg, Germany. [22]Comprehensive Cancer Center (CCC) Mainfranken, Würzburg, Germany. [23]nstitute for Neuropathology, University Medical Center of the Johannes Gutenberg University Mainz, Mainz, Germany. [24]Institute of Neuropathology, Faculty of Medicine, University of Freiburg, Freiburg, Germany. [25]Berta-Ottenstein-Programme for Advanced Clinician Scientists, Faculty of Medicine, University of Freiburg, Freiburg, Germany. [26]Institute for Neuropathology, University of Magdeburg, Magdeburg, Germany. [27]Department of Neuropathology, Institute for Pathology and Neuropathology, University Medical Center Tuebingen, Tuebingen, Germany. [28]Institute for Neuropathology, University Medical Center Goettingen, Goettingen, Germany. [29]Institute of Neurology (Edinger Institute), University Hospital, Frankfurt Cancer Institute (FCI) and University Cancer Center (UCT) Frankfurt, Frankfurg, Germany. [30]German Cancer Consortium (DKTK), Partner Site Frankfurt/Mainz and German Cancer Research Center (DKFZ), Heidelberg, Germany. [31]Department of Neuropathology, Institute for Pathology, Hannover Medical School, Hannover, Germany. [32]Institute for Pathology, University Medical Center Carl Gustav Carus, Technical University Dresden, Dresden, Germany. [33]Department for Radiotherapy, Poliklinik Chemnitz, Chemnitz, Germany. [34]Division of Neuropathology and Neurochemistry, Department of Neurology, Medical University of Vienna, Vienna, Austria. [35]Department of Pediatrics and Adolescent Medicine, Medical University of Vienna, Vienna, Austria. [36]Department of Oncology, University Children's Hospital, Zurich, Switzerland. [37]Children's Research Centre, University Children's Hospital, Zurich, Switzerland. [38]Division of Pediatric Hematology and Oncology, Department of Pediatrics and Adolescent Medicine, Medical University of Graz, Graz, Austria. [39]Department of Pediatric Hematology and Oncology, University Children's Hospital Wuerzburg, Wuerzburg, Germany. [40]Department of Pediatric Hematology and Oncology, University Children's Hospital Wuerzburg, Wuerburg, Germany. [41]Department of Paediatric Haematology/Oncology, Children Medical Hospital, University of Bonn, Bonn, Germany. [42]Department of Pediatrics, Obstetrics and Gynecology, Division of Pediatric Hematology and Oncology, University Hospital of Geneva, Geneva, Switzerland. [43]Cansearch Research platform for Pediatric Oncology and Hematology, Faculty of Medicine, Department of Pediatrics, Gynecology and Obstetrics, University of Geneva, Geneva, Switzerland. [44]Department of General Pediatrics and Pediatric Hematology/Oncology, University Children's Hospital, Oldenburg, Germany. [45]Paediatric Haematology and Oncology, Paediatrics III, University Hospital of Essen, Essen, Germany. [46]Institute of Biostatistics and Clinical Research, University of Muenster, Muenster, Germany. [47]Department of Radiation Oncology, University of Leipzig, Leipzig, Germany. [48]Institute of Neuropathology, Brain Tumor Reference Center of the German Society for Neuropathology and Neuroanatomy (DGNN), University of Bonn Medical Center, Bonn, Germany. [49]Department of Pediatric Hematology and Oncology, Heidelberg University Hospital, Heidelberg, Germany

PURPOSE: To assess outcomes and biological parameters of children younger than 4 years with metastatic medulloblastoma treated within the MET-HIT2000-BIS4 trial or outside the protocol. PATIENTS AND METHODS: 48 trial participants received either carboplatin/etoposide (years 2001 to 2005, n=18) or an intensified Head-Start-based induction (years 2006 to 2011, n=30), both groups with intraventricular methotrexate, followed by high-dose chemotherapy (HDCT) and/or craniospinal radiotherapy (CSI). In an extended cohort, data of 58 additional were grouped with trial participant data. RESULTS: Trial participants (n=48): After intensified induction, both response (26/27 vs. 10/17 eligible patients, p=0.003), and progression-free survival (PFS, 5-year-PFS (5y-PFS): 57% vs 28%, p=0.014) was higher after intensified induction. However, CSI- /progression-free survival (CSIfPFS) was low (5-year CSIfPFS 17%). Biological subtype influenced 5y-CSIfPFS with 3% in non-WNT/non-SHH medulloblastoma vs. 58% in SHH-medulloblastoma (p<0.001), independent of induction regimens. Extended cohort (n=48 on trial and n=58 off trial): Non-WNT/non-SHH medulloblastoma (n=74, all treated in analogy to the MET-HIT2000-BIS4 protocol): Most frequent subtypes were II (5y-PFS 0%, 5y-OS 7%, n=21) and IV (5y-PFS 55%, 5y-OS 57%, n=16). 5y-CSIfPFS was only 8% [n=5]. Among patients in CR (n=13) or PR (n=10), who received HDCT but not CSI in primary therapy, only 5 were CSI-free survivors (CR: n=4/PR: n=1; Subtype III: n=1, Subtype IV: n=2, non-WNT/non-SHH by histology: n=2). SHH-medulloblastoma (n=32, treated with MET-HIT2000-BIS4 [n=16] or HIT2000-BIS4/HIT-SKK chemotherapy [with intrventricular methotrexate, without HDCT; n=16]): 5y-PFS (72%) and 5y-CSIfPFS (69%) did not differ according to therapy or SHH-subgroups. Two therapy-related deaths occurred on MET-HIT2000-BIS4 therapy. Relapses were more frequent after HIT-SKK (p=0.083). CONCLUSIONS: Despite maximally intensified chemotherapy, patients with metastatic non-WNT/non-SHH medulloblastoma almost always require craniospinal radiotherapy to survive their disease. In SHH-activated medulloblastoma, HDCT might better control the disease but careful vigilance of toxicity is important.

MEDB-05. SURVIVAL AND PROGNOSTIC FACTORS IN CHILDHOOD MEDULLOBLASTOMA: A CHINA SINGLE CENTER EXPERIENCE FROM 2006 TO 2015

zhuangzhuang Liang[1], liangliang Cao[2], yang Zhao[2], baocheng Wang[2], shuaiwei Tian[2], jiajia Wang[2], jie Ma[2]; [1]Xinhua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine, shanghai, China. [2]Xinhua Hospital Afiliated to Shanghai Jiao Tong University School of Medicine, shanghai, China

OBJECTIVE: Medulloblastoma (MB) is a malignant embryonal tumor that develops especially in childhood, with overall survival (OS) at 5 years of up to 70%. The aim of the study is to explore the clinical profile and