Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
CoV-2 infection during the same period 4.3% (95%CI; 3.6-5.2) p<0.001. Among 653 patients receiving active cancer therapy during this period, 24 (3.7%) developed COVID-19 and required admission, 4.2% of were receiving chemotherapy, 9.5% immunotherapy and 2.1% targeted therapies. Lung and breast cancer were the most frequent (26.1%), followed by colorectal (19.6%) and breast cancer. No significant differences due to the cancer treatment received were observed. Mortality in lung cancer patients was the highest (25%). The univariate analysis (between p who developed serious event vs. those who did not), showed that higher BrescIA, CURB-65 scale, lactate dehydrogenase (LDH) or C-reactive protein (CRP) levels at admission, the greater risk of developing severe complications (p<0.05).

Conclusions: Patients with cancer, especially lung cancer, and SARS-CoV2 infection have a worse overall prognosis than the general population. Objective parameters such as LDH, CRP at admission, BrescIA index or CURB-65 should alert us to a more serious evolution and suggest early an early intensive care unit (ICU) admission.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2020.08.1797

Table: 1734P Univariate analysis of risk factors for mortality in COVID-19

| Variable                  | Alive | Dead | p-value |
|---------------------------|-------|------|---------|
| Age (years)               |       |      |         |
| South Asian ethnicity     | 67.0  | 7.5  | <0.01   |
| Cardiovascular disease    | 16/16 | 0.8  | 0.03    |
| Cerebrovascular disease   | 23/11 | 0.2  | 0.02    |
| Chronic kidney disease    | 7/8   | 0.8  | 0.02    |
| Hypertension              | 92/46 | 68/58| <0.05   |

* shown as n/%. 1 shown as median (IQR).

Conclusions: Along with known risk factors, cancer confers an independent risk for mortality in COVID-19. Taken together, our findings support the need to continue shielding’ patients with cancer from exposure to COVID-19 infection. Increasing age and co-morbidity should take precedence when weighing up risk factors for severe COVID-19 infection in cancer patients.

Legal entity responsible for the study: University College London Hospitals NHS Foundation Trust.

Funding: Has not received any funding.

Disclosure: H.M. Shaw; Advisory/Consultancy, Speaker Bureau/Expert testimony: Novartis, BMS, MSD; Advisory/Consultancy: ImmunoCore, Idera, Iovance, Genmab, Sanofi Genzyme/Ragenon, Macrogenics, Roche; Speaker Bureau/Expert testimony: Sanofi Genzyme. All other authors have disclosed no conflicts of interest.

https://doi.org/10.1016/j.annonc.2020.08.1798

SARS-CoV-2 infection induces EMT-like molecular changes, including ZEB1-mediated repression of the viral receptor ACE2, in lung cancer models

C.A. Stewart1, C. Gay1, K. Ramkumar1, K.R. Cargill2, R. Cardnell1, M. Nilsson1, S. Heekie1, E.M. Park1, S. Kundu1, L. Diao2, Q. Wang1, L. Shen1, Y. Xu1, C.M. Della Corte1, K. Kundu1, D.L. Gibbons1, J. Wang1, J.V. Heymach1, L.A. Byers1

1Thoracic Head and Neck Medical Oncology, The University of Texas M. D. Anderson Cancer Center, Houston, TX, USA; 2Bioinformatics and Computational Biology, The University of Texas M. D. Anderson Cancer Center, Houston, TX, USA; 3Department of Bioinformatics and Computational Biology, The University of Texas M. D. Anderson Cancer Center, Houston, TX, USA; 4Oncology, University of Campania “Luigi Vanvitelli”, Naples, Italy

Background: SARS-CoV-2 infection is the cause of the respiratory illness COVID-19, which presents most frequently with respiratory symptoms. SARS-CoV-2 cell entry requires interactions with ACE2 and TMPRSS2 on the surface of the host cell. Cancer patients and, specifically, those with thoracic malignancies seem to experience poorer clinical outcomes.

Methods: We utilized bulk and single-cell transcriptional data from a combination of normal and malignant tissues and cells from aerodigestive and respiratory tracts to explore mechanisms governing the expression of ACE2 and TMPRSS2. Additionally, we determined the effect of EMT induction, ZEB1 modulation, and SARS-CoV-2 infection on ACE2 expression.

Results: Our bulk data suggests that aerodigestive and lung cancer models express a broad range of ACE2 and TMPRSS2, particularly in epithelial cells, and would serve as good models for studying SARS-CoV-2 infection. We assessed the relationship between ACE2 and epithelial differentiation in numerous datasets, and found consistent positive correlations with transcriptional and microRNA signifiers of epithelial differentiation. The miR-200 family — zinc finger E-box-binding homeobox 1 (ZEB1) pathway, which is an established regulator of EMT, also directly regulates ACE2 expression. Importantly, ZEB1 is likely via putative ZEB1 repressor sites located in the ACE2 promoter. Furthermore, SARS-CoV-2 infection reduces ACE2 expression and shifts cells to a more mesenchymal phenotype with loss of EPCAM and upregulation of ZEB1 and other EMT-associated genes.

Conclusions: ACE2-positive cells are almost exclusively epithelial and unexpectedly rare, considering the devastating impact of this infection. Following viral entry, SARS-CoV-2 infection induces molecular changes within the cells that are reminiscent of EMT, including increased ZEB1. ZEB1, in turn, appears to directly repress the expression of ACE2. This SARS-CoV-2-induced ACE2 deficiency, compounded by the downregulation of genes, including claudins, which play a critical role in restricting epithelial and endothelial permeability, exposes respiratory cells to increased risk of edema and acute respiratory distress syndrome (ARDS).

Legal entity responsible for the study: The authors.

Funding: NIH/NCI R01-CA207295 (L.A.B.), NIH/NCI U01-CA213273 (L.A.B., J.V.H.), CCSG P30-CA01667 (L.A.B.), University of Texas SPORE in Lung Cancer PS-CA070907 (L.A.B., D.L.G., J.V.H., C.M.G.), the Department of Defense (LC107171; L.A.B.), Khalifa Bin Zayed Al Nahyan Foundation (C.M.G.), RP170067 (EMP), through generous philanthropic contributions to The University of Texas MD Anderson Cancer Center Moon Shot Program and Andrew Sabin Family Fellowship, and The Rexanna Foundation for Fighting Lung Cancer.

Disclosure: C. Gay: Research grant/Funding (self): Astra Zeneca. J.V. Heymach: Advisory/Consultancy, Research grant/Funding (self): AstraZeneca; Advisory/Consultancy, Research grant/Funding (self): GenMab; Advisory/Consultancy, Research grant/Funding (self): Guardant Health; Advisory/Consultancy, Hengrui; Advisory/Consultancy, Spectrum. L.A. Byers: Advisory/Consultancy, Research grant/Funding (self): Astrazeneca; Advisory/Consultancy, Research grant/Funding (self): Biovitrum; Advisory/Consultancy, Research grant/Funding (self): GenMab; Advisory/Consultancy, Genentech; Advisory/Consultancy, Research grant/Funding (self): Genentech; Advisory/Consultancy, Bristol Myers Squibb; Advisory/Consultancy, Genentech; Advisory/Consultancy, Pfizer; Research grant/Funding (self): Tolerol Pharmaceuticals. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2020.08.1799

Elevated AXL expression following SARS-CoV-2 infection in non-small cell lung cancer

K. Ramkumar1, C.A. Stewart1, C. Gay1, R. Cardnell1, L. Diao2, Q. Wang1, L. Shen1, Y. Xu1, S. Kundu1, C. Della Corte1, D.L. Gibbons1, J. Wang1, J.V. Heymach1, L.A. Byers1

1Department of Thoracic/Head and Neck Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; 2Department of Bioinformatics and Computational Biology, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; 3Department of Precision Medicine, University of Campania “Luigi Vanvitelli”, Naples, Italy

Background: Patients with thoracic cancers affected by the coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), have shown poor clinical outcomes. AXL, a TAM (Tyro3, Axl, Mer) family receptor tyrosine kinase, is a known mediator of epithelial to mesenchymal transition (EMT) and therapeutic resistance in non-small cell lung cancer (NSCLC) and other cancers. Additionally, AXL plays a role in efficient Ebola and Zika viral entry and...
infection and AXL inhibition has demonstrated antiviral activities. Recently, bemcentinib, a highly selective and potent AXL inhibitor with antiviral activity, has been fast-tracked as the first potential treatment for assessment in the United Kingdom's ACCELERATING COVID-19 Research & Development (ACCORD) multicenter, randomized phase II trial.

Methods: We analyzed mRNA expression of AXL and other TAM family members as well as angiotensin-converting enzyme 2 (ACE2), the SARS-CoV-2 receptor, in treatment-naïve (n = 1016) and previously treated (n = 239) NSCLC tumors and in a panel of NSCLC cell lines (n = 70). We also analyzed AXL mRNA levels in NSCLC cell lines (n = 3) infected with SARS-CoV-2.

Results: In treatment-naïve and previously treated NSCLC tumors, AXL mRNA expression was higher in mesenchymal tumors, as expected, and inversely correlated with ACE2. Similarly, in NSCLC cell lines, high ACE2 expression was associated with low AXL mRNA and protein expression. Notably, expression of ACE2 was downregulated while that of AXL and ZEB1, an EMT transcription factor, were upregulated in NSCLC cells infected with SARS-CoV-2 as compared to mock infected cells, suggesting a shift to a more mesenchymal phenotype. Treatment with bemcentinib for 24 h downregulated ZEB1 expression in mesenchymal cell lines, reversing EMT.

Conclusions: These data, in the context of ACE2’s role in preventing acute respiratory distress syndrome, suggest a shift from ACE2-expressing epithelial cells to a more mesenchymal phenotype characterized by low ACE2 and high AXL expression, upon infection of NSCLC cells with SARS-CoV-2. In addition to bemcentinib’s antiviral activity, it can also reverse EMT, further supporting AXL and EMT as novel therapeutic targets for COVID-19 treatment.

Legal entity responsible for the study: Lauren A. Byers.

Disclosure: C. Gay: Research grant/Funding (self): AstraZeneca. D. Gibbons: Advisory/Consultancy, Research grant/Funding (self): AstraZeneca, Advisory/Consultancy: GlaxoSmithKline, Advisory/Consultancy: Sanofi; Advisory/Consultancy, Research grant/Funding (self): Janssen; Research grant/ Funding (self): Takeda; Research grant/Funding (self): Pfizer; Research grant/Funding (self): Boehringer Ingelheim; Advisory/Consultancy: Exelixis; Advisory/Consultancy: Genentech; Advisory/Consultancy, Research grant/Funding (self): GlaxoSmithKline; Advisory/Consultancy: Guardant Health; Advisory/Consultancy: Hengrui; Advisory/Consultancy: Lilly; Advisory/Consultancy: Novartis; Advisory/Consultancy, Research grant/Funding (self): licensing/Royalties: Spectrum; Advisory/Consultancy: EMD Serono; Advisory/Consultancy: Kyowa; Research grant/Funding (self): Bayer. L.A. Byers: Advisory/Consultancy, Research grant/Funding (self): AstraZeneca; AbbVie; GenMab; Sierra Oncology; Advisory/Consultancy: BergenBio; Pharma Mar SA; Merc; Bristol Myers Squibb; Genentech; Pfizer; Research grant/Funding (self): Tolerans Pharmaceuticals. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2020.08.1800

Table: 1737P

| Component | Recommendations N | National Guidelines completely compliant to all recommendations N (%) | National Guidelines partially compliant to all recommendations N (%) | No National guidelines about the component N (%) |
|-----------|-------------------|---------------------------------------------------------------------|------------------------------------------------------------------|-----------------------------|
| Patients management | 5 | 7 (53.8) | 5 (38.5) | 1 (7.7) |
| HCW Management | 7 | 4 (30.8) | 8 (61.5) | 1 (7.7) |
| Facility Management | 6 | 7 (53.8) | 5 (38.5) | 1 (7.7) |
| Testing for COVID-19 | 3 | 9 (69.2) | 3 (23.1) | 1 (7.7) |
| Measures to reduce hospital visits | 7 | 6 (46.15) | 6 (46.15) | 1 (7.7) |
| Measures to reduce complications | 2 | 4 (30.8) | 3 (23.1) | 6 (46.1) |
| Five Site specific recommendations | 1 | 7 (53.8) | 0 (0) | 6 (46.1) |

1737P National approaches to managing cancer care: Responses of countries in the MENA region to COVID-19 pandemic

Z. Benbrahim1, M. Al Asiri2, B. Al Bahrami2, M.A.M.A. Al Nassar3, H.O. Al Shamsi2, A. Bounedjar, N. El Saghiri, Z. Fahed2, S. Khatib, O.M.R. Khoshidid1, S. Labidi1, N. Melias1, L. Mula-Hussain1, A. Saleh Hadi Saeed1, A. Iazieh1

1Medical Oncology, Hassan II University Hospital, Fez, Morocco; 2Radiation Oncology, King Fahad Medical City – (KFMC), Riyadh, Saudi Arabia; 3Medical Oncology, National Oncology Center, Royal Hospital, Muscat, Oman; 4Oncology, Kuwait Cancer Control Center, Kuwait, Kuwait; 5Medical Oncology, University Of Sharjah, Sharjah, United Arab Emirates; 6Medical Oncology, CHU de Bilida, Bilida, Algeria; 7Oncology, American University of Beirut Medical Center, Beirut, Lebanon; 8Medical Oncology, St Louis Hospital, Dar Al Shifa Hospital, Damascus, Syria; 9Oncology Department, Jordan University Hospital, Amman, Jordan; 10Medical Oncology, National Cancer Institute - Cairo University, Cairo, Egypt; 11Medical Oncology, Abderrahmen Mami Hospital, Ariana, Tunisia; 12Radiation Oncology, Al-Andalus Oncology Hospital, Bagdad, Iraq; 13Clinical Oncology, National Oncology Center, Aden, Yemen; 14Oncology Department, NGH-National Guard Health Affairs, Riyadh, Saudi Arabia

Background: COVID-19 pandemic presented serious challenge to oncology care due to the associated risks form infection and from disruption of care delivery. Therefore, many professional societies published recommendations to help manage cancer care during the crisis. The objective of our study was to assess the national responses of MENA countries in terms of publishing relevant guidelines and analyse various components of these guidelines.

Methods: A survey based on literature review regarding cancer care adaptation was developed then completed by senior oncologists representing the following countries: Algeria, Egypt, Iraq, Jordan, Kuwait, Lebanon, Morocco, Oman, Saudi Arabia, Syria, Tunisia, UAE and Yemen. The survey queried about instructions of the national recommendations regarding (3) general measures of COVID-19 prevention in oncology, (2) cancer care adaptations during the pandemic.

Results: Analysis of the guidelines revealed 31 essential recommendations categorized into seven essential components with specific recommendations for each component. These components are patients’ management, health care workers (HCW) management, facility management, testing for COVID-19, measures to reduce hospital visits, measures to reduce complications, and site-specific recommendations. The table showed compliance of these guidelines with having the required components and relevant recommendations.

Conclusions: There is inconsistency in the components of the guidelines across the region, which may reflect the evolving nature of the pandemic and lack of clear evidence for many issues in question. There is a need from clear framework on essential components to be included in the guidelines to assure providing the best guidance to the oncology community.

Editorial acknowledgement: On behalf of the International Research Network on COVID-19 Impact on Cancer Care (IRN-CICC).

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: M.A.M.A. Al Nassar: Research grant/Funding (institution): Roche. A. Iazieh: Research grant/Funding (institution): MSD. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2020.08.1801